THE ACYLATION OF CYCLOPROPANES

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RICHARD H. SCHLOSBERG
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This is to certify that the

thesis entitled

THE ACYLATION OF CYCLOPROPANES

presented by

Richard H. Schlosberg

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Chemistry

Harold Hart
Major professor

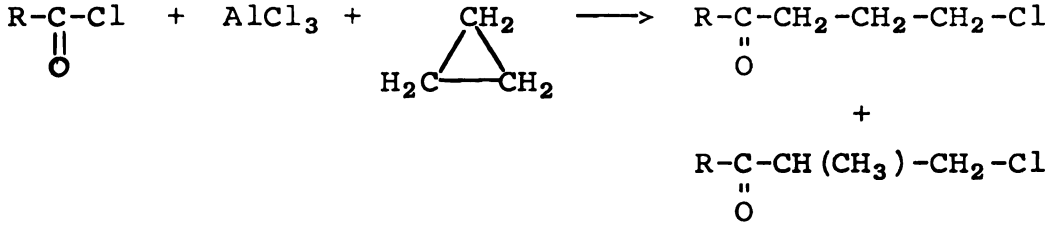
Date August 16, 1967

ABSTRACT

THE ACYLATION OF CYCLOPROPANES

by Richard H. Schlosberg

The Friedel-Crafts acylation of cyclopropane was previously (1) found to proceed smoothly at 0^0 to give a 60 to 80% yield of a mixture of two isomeric chloroketones. These products were shown to be the anticipated γ-chloroketones, and the unexpected, rearranged β-chloroketones, with the latter product predominating.

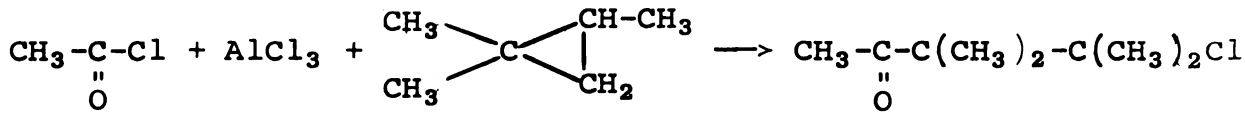


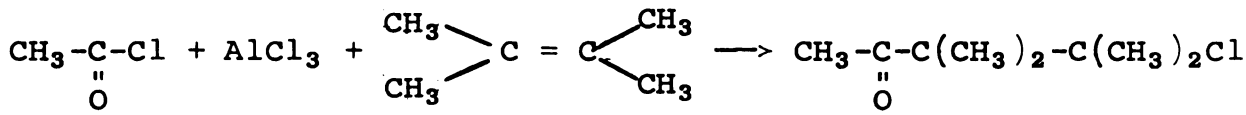
Since the earlier work was carried out before the era of vapor phase chromatography and nuclear magnetic resonance spectroscopy, it was the purpose of this work to re-examine the scope and generality of this reaction with the aid of these techniques. It was also hoped that with these modern methods some light would be shed on the mechanism by which the unanticipated β-chloroketones were produced.

Treatment of cyclopropane with a 1:1 acetyl chloride-aluminum chloride complex in chloroform at 5^0 gave after work-up: 4-chloro-3-methyl-2-butanone, 3-methyl-3-butene-2-one, 5-chloro-2-pentanone, and 3-chloro-2-pentanone in the ratio of 42:31:23:4. The overall yield of acylation

product was 96%. The proposed intermediacy of edge-protonated cyclopropane species readily accounts for these products, and variations in product ratios with reaction conditions support the mechanism.

Several substituted cyclopropanes were investigated. The reaction of 1,1-dimethylcyclopropane with acetyl chloride afforded 4-chloro-3,4-dimethyl-2-pentanone in 78% yield and 3,4-dimethyl-3-pentene-2-one in 22% yield. 1,1,2-Trimethylcyclopropane smoothly reacted in the acylating medium to produce 4-chloro-3,3,4-trimethyl-2-pentanone in 80% yield. The identical chloroketone was also prepared from 2,3-dimethyl-2-butene and acetyl chloride.





2-Ethyl-1,1-dimethylcyclopropane and 2,3-dimethyl-2-pentene were acylated under identical conditions using stannic chloride as the Lewis acid catalyst. The reaction mixtures from the two acylations were found to be quite complicated, but were virtually identical. Thus, it appears that a dialkyl-substituted cyclopropane opens to a tertiary carbonium ion which may isomerize to the most stable olefin prior to acylation.

Richard H. Schlosberg

Methylcyclopropane was acylated to three major products: 4-chloro-2-hexanone (65%), 4-chloro-3-methyl-2-pentanone (18%), and 3-methyl-3-pentene-2-one (12%). A rationalization for the mode of formation of these reaction products, *via* protonated cyclopropanes, is presented.

Phenylcyclopropane was readily acetylated to *p*-cyclopropylacetophenone in 75% yield and 1-(4-acetylphenyl)-2-chloropropane in 15% yield. Thus the benzene ring is attacked more readily than the cyclopropane ring. *p*-Cyclopropylacetophenone furnished the same substituted chloropropane when treated with the acetylating reagent. Both products can be envisioned as arising from initial attack of an acyl cationic species at the para-position of the benzene ring. This leads to an ion which can deprotonate to *p*-cyclopropylacetophenone or suffer nucleophilic attack to furnish 1-(4-acetylphenyl)-2-chloropropane. However, the substituted chloropropane may arise in another manner; *i.e.*, as an acylation product of *p*-cyclopropylacetophenone.

(1) H. Hart and O. E. Curtis, Jr., *J. Am. Chem. Soc.*, **78**, 112 (1956).

THE ACYLATION OF CYCLOPROPANES

By

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To Pamela

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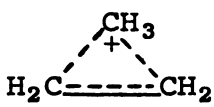
PART A

PROTONATED CYCLOPROPANES FROM THE n-PROPYL SYSTEM

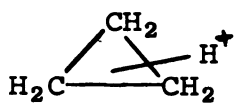
Reports of the intimate association of a proton with a three-membered ring (protonated cyclopropane) occur repeatedly. The importance of such ions, generated from ring closure of the n-propyl system will be discussed in this section of the thesis.

Protonated cyclopropanes have been postulated to have three different structures, 1-3 . Since this carbonium ion has not yet been observed as a stable species, but only



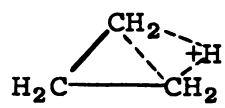
Methyl bridged "Ethylenonium ion"

1



"Face-protonated" Cyclopropane

2



"Edge-protonated" Cyclopropane

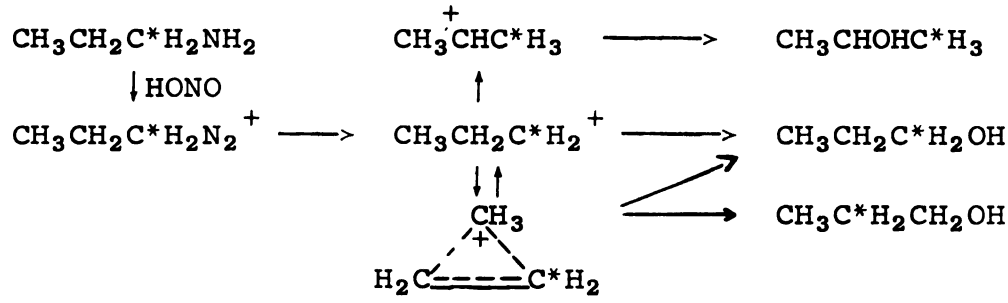
3

postulated as a reaction intermediate, it is not known which structure (or structures) is correct; see however, Part C of this introduction. The two most potent weapons used to secure evidence for the existence of a protonated cyclopropane have been isotopic labelling and trapping of the carbonium ion with a nucleophile.

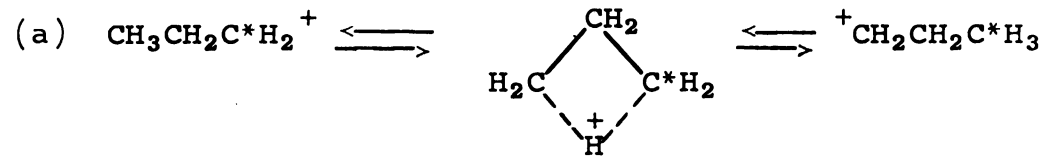
Five groups of workers have reported on the nitrous acid deamination of n-propylamine. Roberts and Halmann (1)

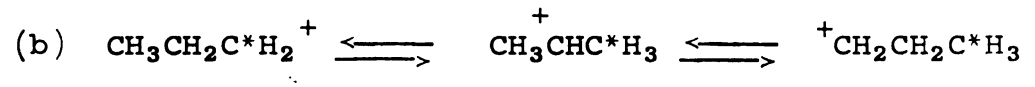
noted that the n-propyl alcohol obtained from the reaction of 1-aminopropane-1-^{14}C with nitrous acid contained 8.5% of isotope-position rearranged product (label at C-2). Scheme I gives Roberts' postulated mechanism for the rearrangement. Oxidation of the 1-propanol with acid permanganate followed by hydrazoic acid treatment gave ethylamine containing 8.5% of the label. On the basis of his reaction mechanism Roberts argued that this 8.5% of the label was entirely on C-2.

SCHEME I

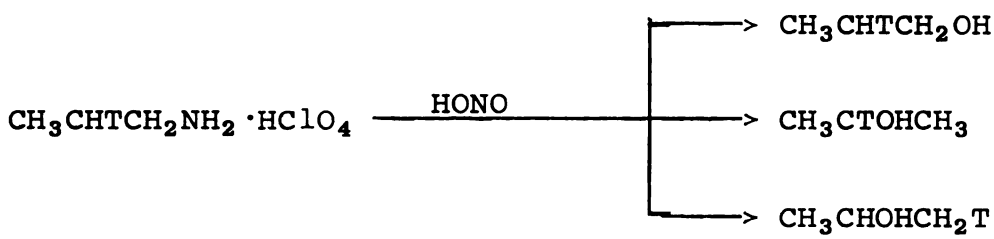


Reutov and Shatkina (2), who repeated this experiment, determined that the activity was in fact on the methyl group of the ethylamine. Reutov suggested two possible modes of rearrangement: (a) a 1,3-hydride shift, or (b) two successive 1,2-hydride shifts. Use of a tritium label on C-2 of





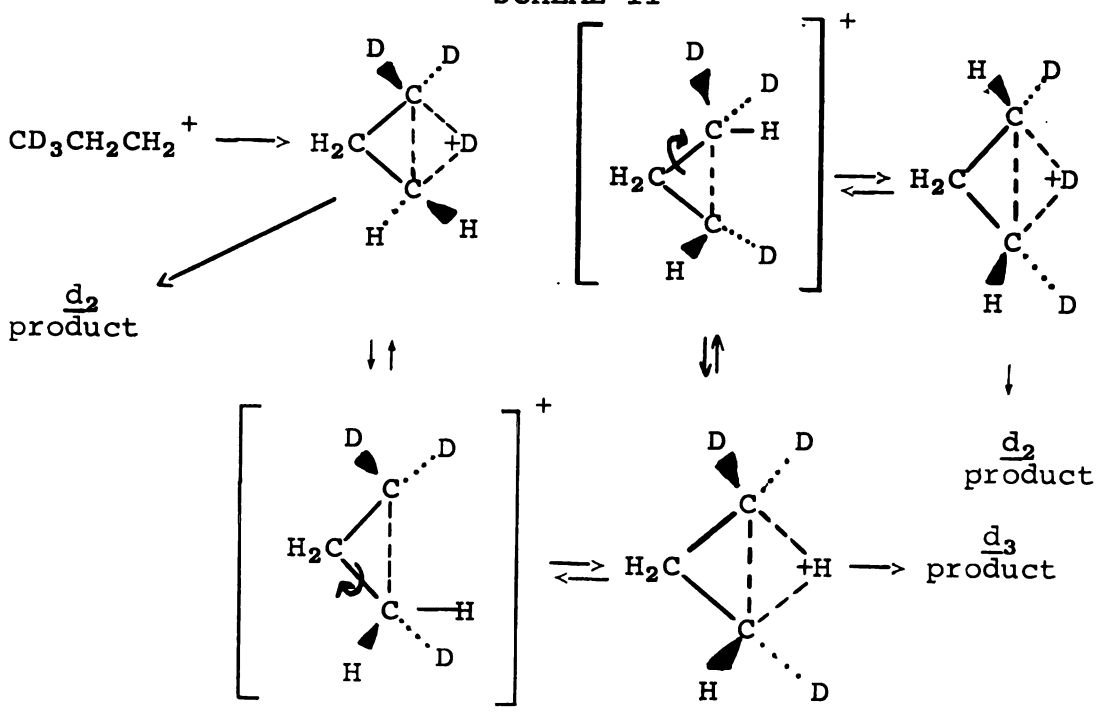
the propylamine excluded the second pathway (3). Here it is evident that under the experimental conditions the isopropyl cation does not rearrange to the n-propyl cation. Support



for Reutov's proposed mechanism appeared in 1962. An nmr study using 1,1,2,2-tetradeuteriopropylamine (4) indicated that a mixture of alcohols containing only deuterium at C-2 was produced. On the basis of his/data and other Karabatsos suggested that the 1-propyl cation irreversibly rearranges to the 2-propyl cation, that the 1-propyl cation undergoes a 1,3-hydride shift, but that protonated cyclopropanes are not formed and methyl migration does not occur.

Repudiation of the 1,3-hydride shift mechanism appeared in 1964. Deamination of 3,3,3-$\underline{d}_3$-1-aminopropane (5) was the crucial experiment. Rather than look at the 1-propanol formed, Baird and Aboderin studied the cyclopropane fraction and found 43 ± 1% cyclopropane-$\underline{d}_2$ and 57 ± 1% cyclopropane-$\underline{d}_3$. Invoking formation of a protonated cyclopropane followed by extensive H and D mixing (Scheme II) they statistically calculated 4/7 cyclopropane-$\underline{d}_3$ and 3/7 cyclopropane-$\underline{d}_2$ as the product distribution, in very good agreement with the observed results.

SCHEME II



A paper by Karabatsos, Orzech and Meyerson (6) endorsed Baird's scheme. Equations (1) and (2) display the isotopic distribution of the 1-propanols, as calculated from mass spectrometric fragmentation patterns. At 40^0 approximately

(1) $CH_3CH_2CD_2NH_2 \longrightarrow CH_3CH_2CD_2OH + C_2H_4DCHDOH + C_2H_3D_2CH_2OH$

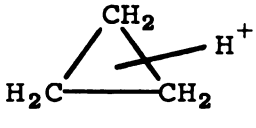
95.7% 1.0% 3.3%

(2) $CH_3CD_2CH_2NH_2 \longrightarrow$ " " "

1.2% 0.9% 97.9%

5% of the 1-propanol was felt to arise via protonated cyclopropanes.

A final word on this controversy concerns two papers (7,8) which lend further credence to the involvement of protonated cyclopropanes. When 1-propylamine-1-^{3}H was deaminated (7), the 1-propanol contained 1.7 ± 0.1% tritium at C-2 and 1.2 ± 0.1% tritium at C-3. 1-Propylamine-1-^{14}C deamination again resulted in 4-6% isotopically scrambled 1-propanol (8). These data led Lee to suggest that the three carbon atoms became equivalent or approached equivalence via protonated cyclopropanes (2 or 3a, 3b, 3c).



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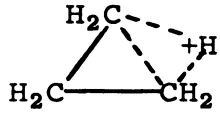
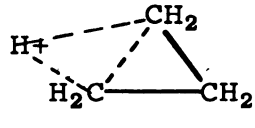
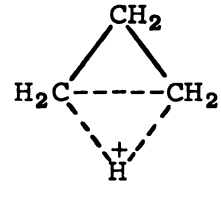


3a



3b



3c

Other reactions involving the n-propyl system have been examined. For example, whereas acetolysis of 1-propyl tosylate-1-^{14}C resulted in no isotopic rearrangement, formolysis of the tosylate afforded 1-2% of rearranged substitution product (9). Lee suggested that the C-2 and C-3 labelled formates arose from "edge-protonated" cyclopropane precursors*.

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*The question of "edge-protonated" vs. "face-protonated" cyclopropanes will be discussed in Part C.

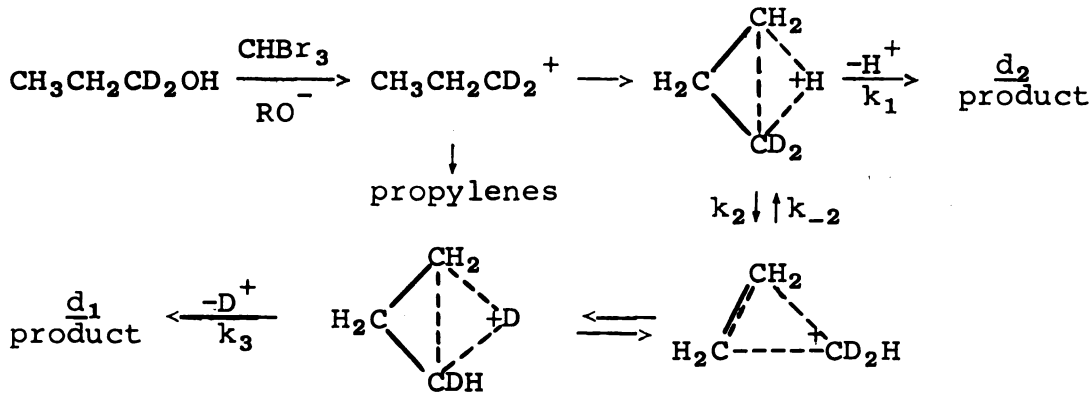
Treatment of alcohols with bromoform and strong base provides products which appear to be typical of carbonium ions (Equations (3) and (4)) (10). n-Propyl alcohol "deox-

$$(3)\quad RO^- + :CBr_2 \longrightarrow Br^- + ROCBr \longrightarrow R^+ + CO + Br^-$$

or

$$(4)\quad RO^- + :CBr_2 \longrightarrow 2Br^- + ROC^+ \longrightarrow R^+ + CO$$

ideates" to cyclopropane. The cyclopropanes from the "deoxideation" of 1,1-d_2-1-propanol (11) were $C_3H_4D_2$ (94 ± 2%) and C_3H_4D (6 ± 2%). Although Skell discounted a protonated cyclopropane intermediate, his results are probably best accounted for by a carbonium ion sequence such as outlined in Scheme II. If the electron-deficient site generated by "deoxideation" is more reactive than that arising from deamination, incomplete scrambling would be expected: the ion would collapse to stable product in a very fast step. Hence the 57:43 ratio observed in the deamination of 3,3,3-d_3-1-propylamine (5) could not be approached. One obtains more cyclopropanes from "deoxideation" than from diazotization reactions (12). Thus, the ions generated from alcohols in the former cases appear less selective (higher in energy) than those derived from amines. It is therefore reasonable to assume that $k_1 > k_2$ and as a result d_2 product predominates in this case. A study of the cyclopropanes formed from the "deoxideation" of 3,3,3-d_3-1-propanol and from the deaminations of 1,1-d_2- and 2,2-d_2-1-propylamine might shed further light on this question.

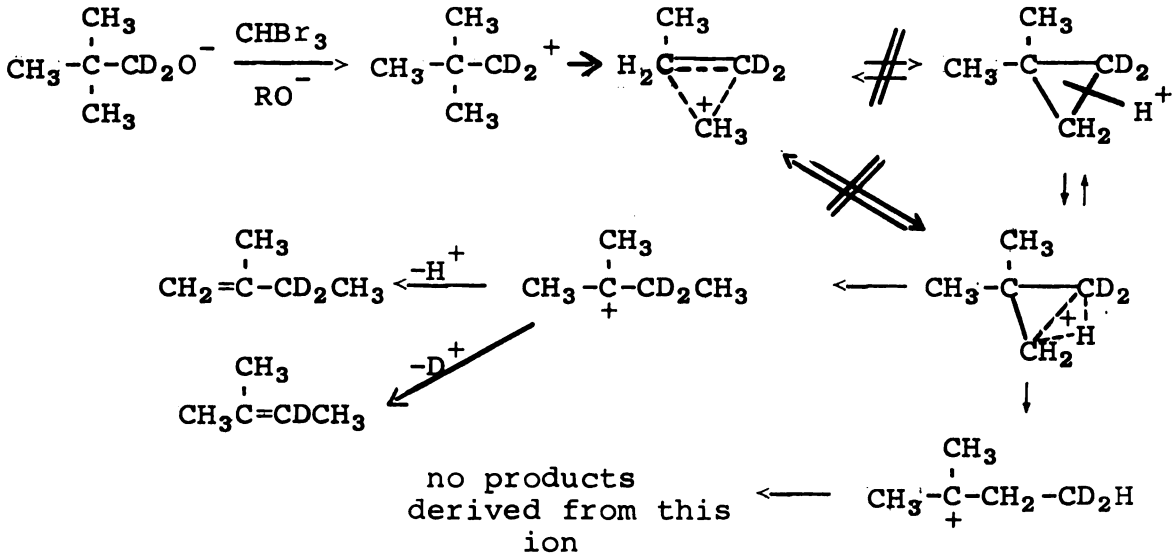


The reactions of n-propyl chloride with hydrogen chloride and zinc chloride (13) and of n-propyl bromide with aluminum bromide (14,15) have been investigated recently. Treatment of 1-propyl chloride-1-^{14}C for 100 hours at 50^0 with a twofold excess of zinc chloride and hydrochloric acid (13) led to 7% 1-propyl chloride-3-^{14}C, designated as a 1,3-hydride shift product. However, since the experimental method for determining the isotope position employed in this case was the same as that used in Reutov's deamination work, this experiment might profitably be repeated. Douwes and Kooyman (14) treated 1-propyl bromide-2,2-d_2 with aluminum bromide in carbon disulfide at -20^0 and recovered only isotopically unrearranged starting material. Treatment of $CH_3CH_2CD_2Br$ with approximately 0.2 molar ratio aluminum bromide for five to six minutes furnished (15) a product with 15-20% isotope position rearrangement. Similar treatment of $CH_3CD_2CH_2Br$ yielded 5-8% rearranged deuterium. 1-Propyl bromide-1-^{13}C led to about 7% label at C-2 and about 13% at C-3. These data require that the bulk of rearranged

1-propyl bromide arise *via* protonated cyclopropane intermediates.

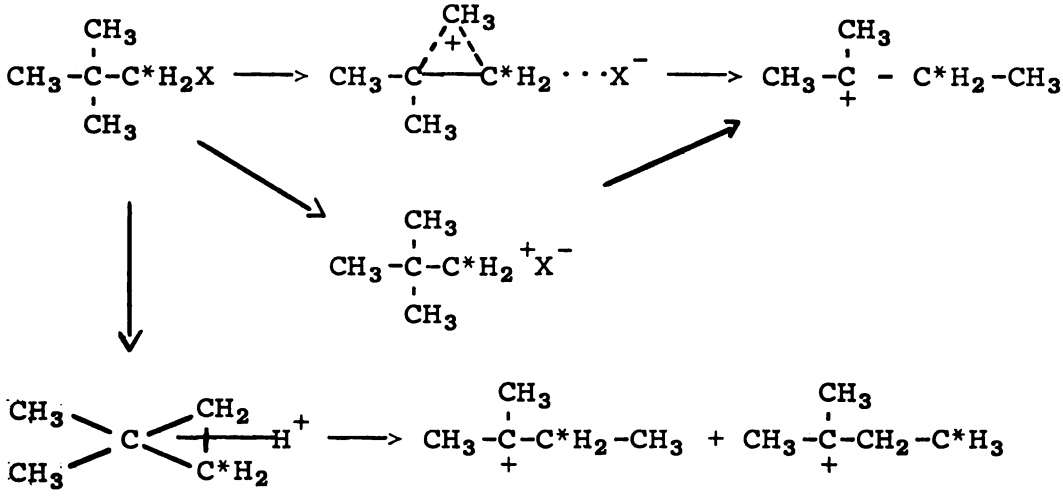
Whereas the route to protonated cyclopropanes is quite rigorously demonstrated in the *n*-propyl system, the neopentyl system does not appear to close to a protonated cyclopropane. Hydrobromination of neopentyl alcohol-1-^{13}C with hydrogen bromide (16) provided only 2-bromo-2-methylbutane-3-^{13}C (Wagner-Meerwein rearrangement product), and none of the 2-bromo-2-methylbutane-4-^{13}C expected if a bridged ion were involved. Neopentyl alcohol-α,α-d_2 with bromoform and strong base (17) "deoxideated" to 2-methyl-1-butene-3,3-d_2 and 2-methyl-2-butene-3-d as the only olefins. Failure to find deuterium on C-4 corroborates the ^{13}C evidence (16) which excludes a protonated cyclopropane (Scheme III).

SCHEME III



Solvolyses of neopentyl-1-^{13}C tosylate and iodide and deamination of neopentyl-1-^{13}C amine produced tert-amyl alcohol with the label confined to the C-3 position (**18**). These results eliminate the involvement of protonated cyclopropanes in these reactions: hydrogen-bridged species, if formed, would lead to product labelled at C-4 as well as at C-3 (Scheme IV).

SCHEME IV



Intermediate cases, the n-butyl and isobutyl systems, display less propensity for a protonated cyclopropane pathway than the n-propyl system and more than the neopentyl system (**19**,**20**,**21**,**22**).

In conclusion, compelling evidence has accumulated supporting the intervention of protonated cyclopropanes to a small but significant degree in carbonium ion rearrangements of species generated from aliphatic precursors. These hydrogen-bridged ions are most important in the n-propyl

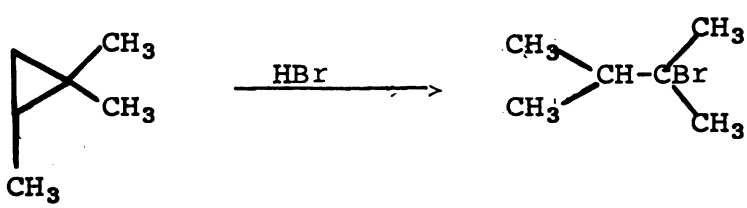
system, become far less prevalent when the alternative classical carbonium ion is secondary, and apparently are not involved when a tertiary carbonium ion may be preferentially formed.

PART B

PROTONATED CYCLOPROPANES FROM CYCLOPROPANE

It has been generally accepted that cyclopropane undergoes simple Markownikov acid cleavage and reacts as an olefin would, albeit somewhat less readily*. The reactions of cyclopropane with sulfuric acid (23), hydrobromic acid (24, 25), and hydrofluoric acid (26), for example, give only n-propyl products. Although some speculation on a protonated cyclopropane intermediate was advanced (25), the first experimental evidence supporting the existence of such bridged ions in electrophilic attack on cyclopropane appeared in 1963. This short note revealed (27) the remarkable observation that when D^+ was added to cyclopropane extensive mixing of the deuteron and the ring protons occurred. In the subsequent full paper (28), Baird and Aboderin disclosed that the average deuterium distribution in the 1-, 2-, and

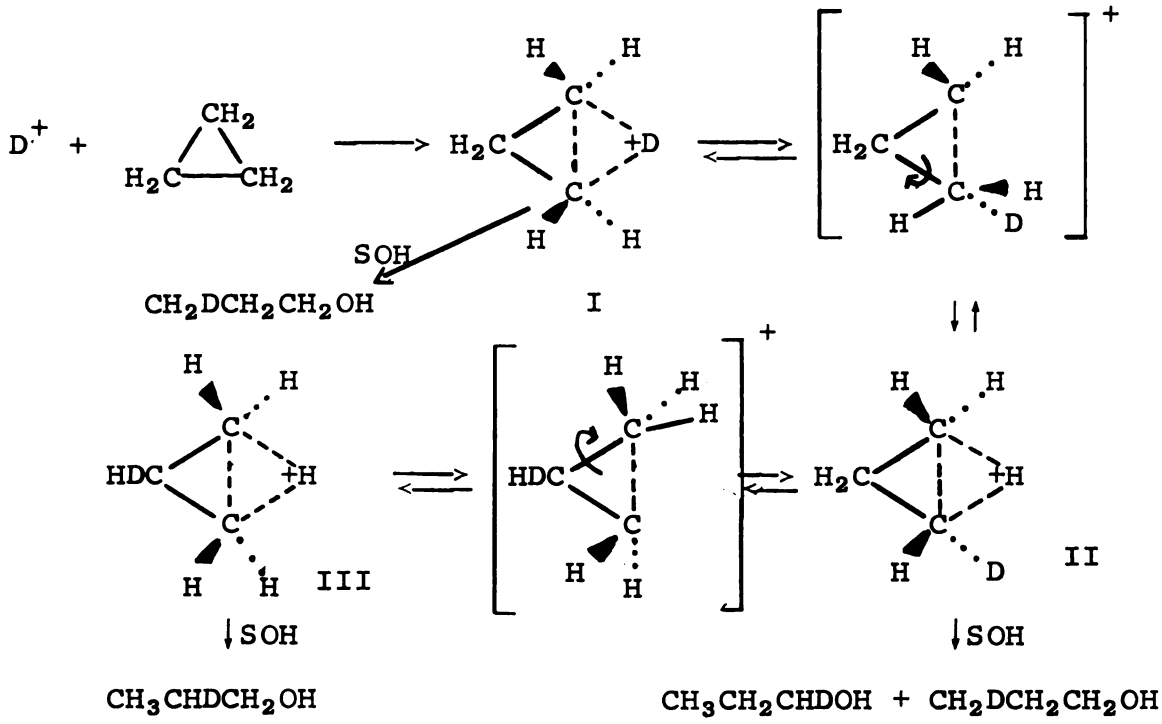
*For example, 1,1,2-trimethylcyclopropane upon treatment with hydrobromic acid yielded only 2,3-dimethyl-2-bromobutane (N. Kizhner and G. Khanin, J. Russ. Phys. Chem. Soc., 45, 1775 (1911); Beil., 5 (I), (1911).



Also see, R. T. Morrison and R. N. Boyd, "Organic Chemistry", Allyn and Bacon, Inc., Boston, 1967, p. 277.

3-positions of the 1-propanol formed from solvolysis of cyclopropane in 57% (8.43M) D_2SO_4 was 0.38, 0.17 and 0.46 deuterium atom respectively. This widespread isotope position rearrangement was interpreted according to Scheme V*.

SCHEME V



The possibility of deuterium scrambling subsequent to formation of the acid sulfate or alcoholic products was excluded. A control experiment demonstrated that 1-propanol-1,1-$\underline{d_2}$ was not affected by conditions (8.43M D_2SO_4 at 50° for one week) considerably more severe than those used

*Actually the equilibration of ions I, II, and III by the rotation of quasi-methyl groups is a variation suggested to Baird by Prof. K. Wiberg. Baird originally invoked methyl-bridged ions.

in ordinary solvolysis (8.43M D_2SO_4 at 25^0 for 10 hours).

When solvolyzed in concentrated acid (96% D_2SO_4) cyclopropane yielded 1-propanol containing equal amounts of deuterium at carbons one and two (29). These data are consistent with those obtained by Baird in his studies (27,28). In 96% acid the bridged ion is relatively free from solvation by water and nucleophilic attack by solvent is quite slow in comparison with the rate of equilibration of protonated cyclopropanes. In the weaker acid system used by Baird and Aboderin there is approximately a 4:1 molar ratio of water to sulfuric acid and the ion formed here consequently undergoes more rapid solvent capture. Therefore scrambling would be expected to be less complete.

Reaction of cyclopropane with benzene and aluminum chloride (30), cyclopropane with benzene and hydrofluoric acid (31) and the cationic oligomerization of isopropylcyclopropane catalyzed by aluminum bromide (32) are but a few examples of the many allied reactions which may involve bridged ions. Much remains to be done before valid proof of protonated cyclopropane formation in these and other reactions* can be demonstrated.

Along with sulfation the standard electrophilic reactions are Friedel-Crafts acylation, Friedel-Crafts alkylation,

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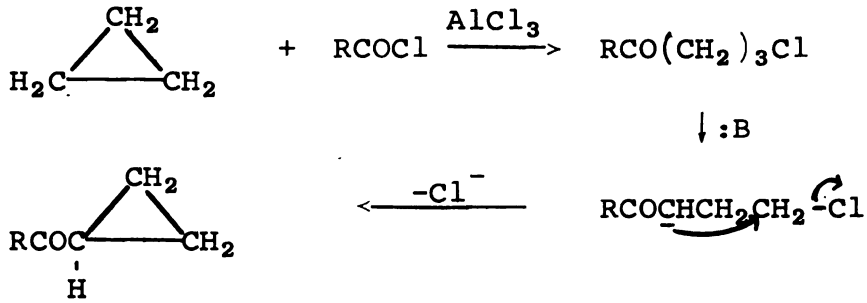
*For example, D. J. Abraham and W. E. Truce, J. Org. Chem., 28, 2901 (1963) reported that treatment of cyclopropane with tosyl chloride and aluminum chloride in methylene chloride at room temperature for 48 hours led to a 32% yield of the 1,3-addition product along with smaller yields of two other products which were not identified (perhaps the 1,2- and 1,1-addition products).

halogenation and nitration. The acylation of cyclopropane under Friedel-Crafts conditions has a long history. When cyclopropane was bubbled into a carbon disulfide solution of an acetyl bromide-aluminum bromide complex (33), a 15-20% yield of a C_5H_8O ketone was reported. The remainder of the material presumably was "Friedel-Crafts tar". Krapivin could not characterize this ketone, although its probable structure was 3-methyl-3-butene-2-one (34).

In a homogeneous solution of acetyl chloride and aluminum chloride in chloroform (34), cyclopropane was rapidly and exothermically absorbed at 0^0. The reaction mixture was subjected to an acid work-up and the crude product refluxed with 20% sodium bicarbonate. Under these conditions Hart and Curtis realized a 36% yield of 3-methyl-3-butene-2-one and a 30% yield of 5-chloro-2-pentanone. From the known chemistry of cyclopropane it was felt that acylation of cyclopropane to the 1,3-addition product followed by base catalyzed dehydrohalogenation would provide a facile synthesis of cyclopropyl ketones (Eq. 5). The formation of

(5) 

3-methyl-3-butene-2-one as the major product was not expected and no plausible mechanism describing its formation was

advanced. Although 4-chloro-3-methyl-2-butanone was not found, its initial formation was inferred from the fact that β-chloroketones of structure 4 were identified as products when cyclopropane was acylated with propionyl chloride (R = C_2H_5) and isobutyryl chloride (R = $(CH_3)_2CH$).

$R-\overset{\overset{O}{\|}}{C}-CH(CH_3)CH_2Cl$

4

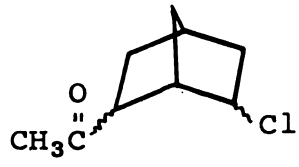
R	Yield of 4 (%)
C_2H_5	39
$(CH_3)_2CH$	34

Furthermore, only 4-chloro-3,4-dimethyl-2-pentanone (5) (49% yield) (35) was isolated from the acylation of

$CH_3COCH(CH_3)C(CH_3)_2Cl$

5

1,1-dimethylcyclopropane. None of the "normal" γ-chloroketone, 5-chloro-5-methyl-2-hexanone was observed. In sharp contrast with the far-reaching rearrangements observed in the acylations of cyclopropane and 1,1-dimethylcyclopropane, nortricyclene afforded the expected 2-chloro-6-acetylnorbornane (6) in 69% yield and no unexpected products (36).



6

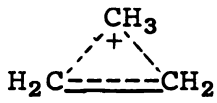
Since the work on cyclopropane acylation (33,34) was carried out before the era of vpc and nmr one purpose of

this investigation was to reexamine the reaction products with the aid of these techniques. Furthermore it was hoped that with the aid of vpc minor products, if present, could be detected, separated and identified. In addition it was hoped that some additional data could be obtained which might shed light on the mechanism of the unusual rearrangement discovered by Curtis (34). These reinvestigations comprise the major part of this thesis, but before the results are presented, the question of "edge" vs. "face"-protonated cyclopropanes will be considered.

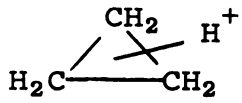
PART C

"EDGE-" vs. "FACE-PROTONATED" CYCLOPROPANES

The structure of protonated cyclopropanes has been discussed in terms of a symmetrical methyl-bridged ion (1), a symmetrical, "face-protonated" species (2), or a species in which the proton is associated with only two carbon atoms of the cyclopropane ring; i.e., "edge-protonated" cyclopropane (3).



1



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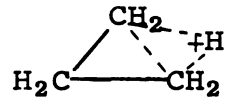
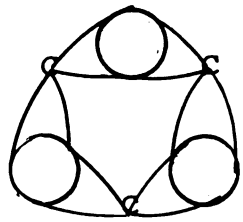


3

Two alternative molecular orbital representations of cyclopropane are the bent-bond model (7) (37) and the Walsh model (8) (38). The optimum configuration for the



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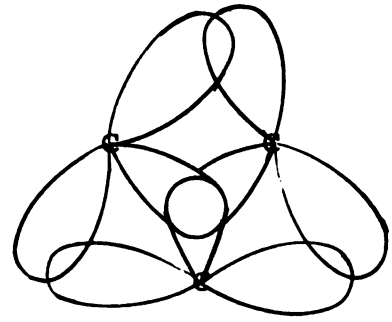


8

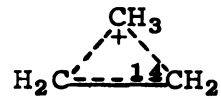
bent-bond model leads to bonds which are "bent" by about 21^0. Addition of a proton to either model of cyclopropane readily leads to either a "face-protonated" or an

"edge-protonated" species. Extended Hückel molecular orbital calculations (39) suggest that the preferred avenue of approach for the addition of a proton to a cyclopropane ring is in the plane of the carbon atoms and in the direction of the center of a carbon-carbon bond; i.e., the "edge-protonated" form 3 (40). This is a case in which theory preceded experimental evidence. Recently, the results from the formolysis of 1-propyl tosylate-1-^{14}C (Eq. 6)

(6) $CH_3CH_2{}^{14}CH_2OTs \xrightarrow{HCOOH} CH_3CH_2CH_2OCOH$

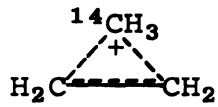
$\%^{14}C$ in product - C-3 (0.68%), C-2 (0.15%)
C-1 (99.17%).

led Lee to suggest (41) that edge-protonated cyclopropanes are the bridged ions which best accomodate the observed isotope-position rearrangement. The first formed methyl-bridged species (9) could lead to product via two pathways (Eq. 7).

(7) $CH_3CH_2{}^{14}CH_2{}^+ \longrightarrow$  $\xrightarrow{k_1} CH_3{}^*CH_2{}^*CH_2OCOH$

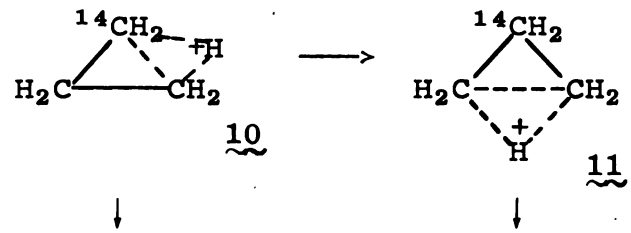
9

$k_2 \downarrow\uparrow$

 $\longrightarrow {}^*CH_3CH_2CH_2OCOH$

If $k_1 > k_2$ more label would be expected at C-2 than at C-3. If $k_1 < k_2$ the label would become equally distributed over all three carbons and the product would have equal amounts of ^{14}C at carbons 2 and 3. Since the product was determined

to contain a greater amount of ^{14}C at C-3 than at C-2 the methyl-bridged ion was discarded as a species which could lead to products. A face-protonated cyclopropane is symmetrical and would lead to an equal amount of label on C-2 and C-3 in the product. It, too, was excluded on the basis of the experimental results. The first formed edge-protonated cyclopropane, 10, however, would give product with more label at C-3 than at C-2. In order to give $CH_3{}^{14}CH_2CH_2OCOH$ 10 must equilibrate to 11 (Eq. 8).

(8) $CH_3CH_2{}^{14}CH_2{}^+$ ⟶  ⟶

10 11

$^{14}CH_3CH_2{}^{14}CH_2OCOH$ $CH_3{}^{14}CH_2CH_2OCOH$

Related studies on the norbornyl system have been conducted and reflect on the situation in the cyclopropyl ion. Ionization of apoisobornyl, exo-camphenilyl and β-fenchoisocamphoryl brosylates (42) led to the observation of anchimeric acceleration via the proposed bridged ions 12 and 13. A 6,1-hydride shift form (edge-protonated) was favored over a 6,2-hydride shift species (face-protonated) in these systems.

12 13

In the solvolysis of exo-norbornyl brosylate the endo-hydrogen at C-6 will migrate to the two possible configurations at C-2 with about equal facility if ion 14 is formed.

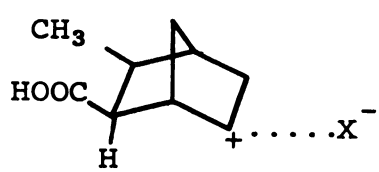
"Nortricyclonium Ion"

14

Exclusively endo-migration will occur if the edge-protonated ion 15 is generated. The intramolecular transannular

15

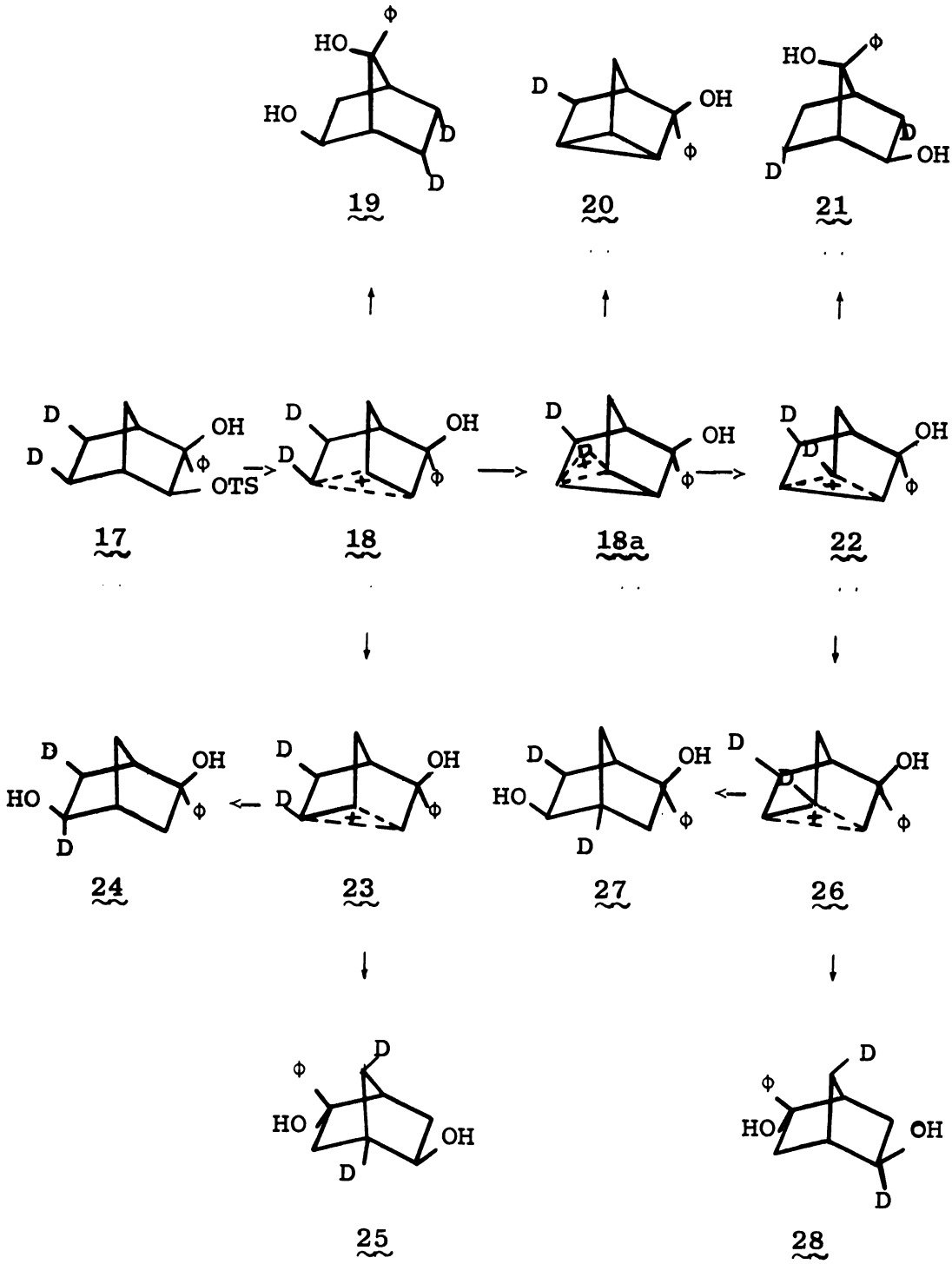
hydride shift of the 2-carboxy-3-methyl-5-norbornyl cation (16) proved to be exclusively endo ⟶ endo (43), thus supporting the existence of ion 15.



16

Hydrolysis of the substituted norbornyl tosylate 17 afforded seven alcohols (44) as outlined in Scheme VI.

SCHEME VI


HO
Φ
HO
D
D
19
D
OH
Φ
20
HO
Φ
D
D
OH
21
D
D
OH
Φ
OTS
17
D
D
OH
Φ
18
D
OH
Φ
18a
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OH
Φ
22
D
HO
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Φ
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24
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Φ
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27
D
D
OH
Φ
26
Φ
HO
D
OH
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25
Φ
HO
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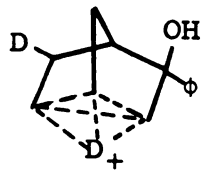
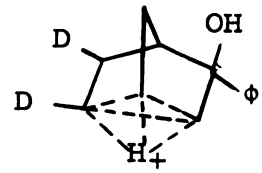
OH
D
28

Species 29 and 30 depict the only reasonable face-protonated and face-deuterated ions derivable from the hydrolysis of 17.



29



30

Collins averred that it is inconceivable that 29 could yield products containing deuterium in the bridgehead positions (e.g., 25,27). He also suggested that 30 does not seem capable of yielding products other than those with deuteriums on adjacent carbons, thereby excluding 21, 27 and 28. Mechanistic employment of edge-protonated forms (e.g., 18a) leads to the ready formation of all alcohols produced. Thus, both on the basis of theoretical considerations (39,40) and experimental evidence (41,42,43,44) edge-protonated structures appear to be the preferred geometries for protonated cyclopropanes.

EXPERIMENTAL

I. General Procedures

All nmr spectra were measured with a Varian A-60 or Jeolco C-60H spectrometer. Chemical shifts are reported as τ values measured from tetramethylsilane or methylene chloride as an internal standard. Analysis by vpc was carried out on columns of 5- or 10-foot lengths, packed with SE-30, 20% on Chromosorb W, FFAP, 20% on Chromosorb W, or SF-96, 20% on Chromosorb P at approximately 130^0. The infrared spectra were obtained on a Unicam Model SP-200 infrared spectrometer and all ir spectra were calibrated using a polystyrene film. All ultraviolet spectra were measured with a Unicam Model SP-800 or a Beckman Model DB spectrophotometer. The mass spectra of the chloroketones arising from the acylation of cyclopropane were obtained by S. Meyerson and E. Bednar, American Oil Company, Whiting, Indiana. Other mass spectra were obtained by Dr. H. Harris and Dr. J. Wettaw of this department with a Consolidated Electrodynamic Corporation 21-103C instrument operating at an ionizing potential of 70 v.

II. The Acylation of Cyclopropane

A. The Friedel-Crafts Acetylation of Cyclopropane

The method of Hart and Curtis (34) was employed in this reaction. A 300-ml, three-necked flask equipped with a dry-ice

condenser, stirrer, gas-inlet tube, and pressure equalizing dropping funnel was cooled by means of an external salt-ice bath. Into a 250-ml, one-necked flask equipped with a magnetic stirrer and dropping funnel, was introduced a mixture of anhydrous aluminum chloride (26.67 g, 0.200 mole) in 50 ml of methylene chloride. A solution of 16.49 g (0.210 mole) of acetyl chloride in 50 ml of methylene chloride was added over a one-hour period. After addition of the acetyl chloride solution the mixture was stirred for an additional hour and then filtered through a scintered glass funnel into the three-necked flask. While the clear, pale yellow solution was maintained below 10^0, cyclopropane (11 ml, 7.9 g, 0.19 mole) was condensed in a trap cooled to -79^0 and bubbled into the acylating medium over a 45 min period. After the addition of the cyclopropane the reaction mixture was stirred for one hour at $3-6^0$. During the time of addition and stirring the solution took on a deep orange-brown color. The reaction mixture was hydrolyzed by slowly pouring it with stirring onto a mixture of 100 ml of concentrated hydrochloric acid and 250 g of crushed ice. The aqueous layer was separated and washed successively with 50-ml portions of water, 10% sodium bicarbonate solution, and water and dried over anhydrous sodium sulfate. After removal of the solvent, the yield of acetylated product was 21.8 g. Vpc analysis on a 5-foot Se-30 column at 115^0 with a Helium flow rate of 40 ml/min indicated that the product consisted of 14% of C_5H_8O (ret. time 0.80 min) and 86% of C_5H_9OCl (ret. times

2.2, 4.8, 7.5 min) material. On this basis there was a 96% yield of monoacylated product. The reaction products were separated by preparative scale vapor phase chromatography. The product with the retention time of 2.2 min was present in 4%, the second chloroketone was formed in 42% and the third in 23% yield.

1. Product Identification

a. 5-Chloro-2-pentanone. This compound had a retention time of 7.5 min and a boiling point of 75-77^0 at 23 mm, literature value (34), 77-78^0 at 22 mm. It was a clear, colorless liquid which quickly darkened and decomposed upon standing at room temperature. Its ir spectrum (liquid film) showed principal bands at 1710 ($\nu_{C=O}$) and 760 cm^{-1} (ν_{C-Cl}). The mass spectrum indicated parent peaks at m/e 120, 122 and peaks at m/e 84 (parent - HCl), 58 ($CH_3C(OH)=CH_2^+$), and 43 (CH_3CO^+). The nmr spectrum (neat) consisted of a sharp singlet at τ 7.89 (3H), a triplet (J = 6.5 cps) at τ 7.38 (2H), a complex multiplet centered at τ 7.89 (2H), and a triplet (J = 6.0 cps) at τ 6.42 (2H), assigned to the protons on C-1, C-3, C-4, and C-5 respectively.

b. 4-Chloro-3-methyl-2-butanone. The retention time of this chloroketone was 4.8 min. It was a clear, colorless liquid which quickly darkened and decomposed overnight at room temperature. The principal ir bands (liquid film)

appeared at 1710 ($\nu_{C=O}$) and 758 cm^{-1} (ν_{C-Cl}). The mass spectrum indicated, in addition to the parent peaks at m/e 120, 122, intense peaks at m/e 85 (parent - Cl), 84 (parent - HCl), and 42 (CH_2CO^+), and no sign of the mass spectrometrically induced rearrangement products characteristic of carbonyl compounds containing γ-hydrogens (45). The nmr spectrum (neat) showed a sharp singlet at τ 7.85 (3H; methyl ketone), complex multiplets centered at τ 7.18 (1H; methine proton) and τ 6.45 (2H; methylene protons), and a doublet (J = 7.0 cps) at τ 8.80 (3H; methyl group on C-3)*.

c. 3-Methyl-3-butene-2-one. The α,β-unsaturated ketone had a retention time of 0.80 min, and a boiling point of 44-45° at 98 mm, literature value (34), 45-46° at 98 mm. It was a clear, colorless liquid with $\lambda_{max}^{95\%EtOH}$ 218 mμ (log ε 3.84), literature value (46), $\lambda_{max}^{95\%EtOH}$ 218 mμ. Its ir spectrum (CCl_4 soln) displayed prominent bands at 1678 ($\nu_{C=O}$) and 1635 cm^{-1} ($\nu_{C=C}$). The nmr spectrum (CCl_4 soln) consisted of a sharp singlet at τ 7.71 (3H; methyl ketone), complex multiplets centered at τ 4.10 (1H; H_{trans}) and τ 4.25 (1H; H_{cis}), and a three line absorbance centered at τ 8.15 (3H; allylic methyl) (47).

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*C-3 is an asymmetric center thereby producing a magnetic nonequivalence of the methylene protons and of the protons of the C-3 methyl group. For a discussion of this phenomenon see, G. M. Whitesides, D. Holtz, and J. D. Roberts, J. Am. Chem. Soc., 86, 2628 (1964).

d. 3-Chloro-2-pentanone.

(1) Physical properties. This was the compound with a retention time of 2.2 min. The principal ir bands (liquid film) appeared at 1718 ($\nu_{C=O}$)* and 758 cm^{-1} (ν_{C-Cl}). The mass spectrum had prominent peaks at m/e 120, 122 (parent), 92, 94 ($CH_3C(OH)=CHCl^+$) and 43 (CH_3CO^+). The nmr spectrum (neat) showed a sharp singlet at τ 7.75 (3H), two doublets (J = 7.4 cps) centered at τ 5.96 (1H), a complex multiplet centered at τ 8.12 (2H), and a triplet (J = 7.1 cps) at τ 8.97 (3H)**

(2) Independent synthesis of 3-chloro-2-pentanone. The method of Buchman and Richardson (48) was used in this synthesis. Into a 300-ml, three-necked flask equipped with a magnetic stirrer, thermometer, pressure equalizing dropping funnel and drying tube was introduced a solution of 17.2 g (0.200 mole) of 2-pentanone diluted with 20 ml of dry benzene. Sulfuryl chloride (27 g, 0.20 mole) was dropped into the stirred solution over a period of 20 min while the reaction temperature was maintained below 24^0 by means of external cooling with a water bath. The clear, colorless solution was stirred for an additional 50 min at

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*Halogen substitution in the immediate vicinity of a carbonyl group results in a shift to higher frequency of the carbonyl absorption. For a leading reference see, L. J. Bellamy, "The Infra-red Spectra of Complex Molecules", J. Wiley and Sons, Inc., New York (1958) p. 139.

**See footnote page 26.

22^0, then quickly poured onto approximately 100 g of crushed ice. About 20 ml of methylene chloride was added and the combined organic layers were separated and dried over anhydrous sodium sulfate. After removal of the solvent *in vacuo*, the organic material was vacuum distilled and 4.1 g (17%) of a product with a boiling point of $57-58^0$ at 49 mm, (literature value (48), $62-66^0$ at 56 mm) was collected. This clear, colorless liquid darkened and decomposed slowly upon standing at room temperature, but appeared to be stable indefinitely when kept in the dark at 0^0. This product was found to be identical in all respects (ret. time, ir and nmr spectra) with the acylation product, 3-chloro-2-pentanone.

B. The Acylation of Cyclopropane in Various Solvents

The Friedel-Crafts acylation of cyclopropane was carried out in carbon tetrachloride, chloroform, methylene chloride, carbon disulfide and nitrobenzene, solvents widely used in aliphatic acylations (49). All four products were produced upon the addition of cyclopropane to an acetyl chloride-aluminum chloride complex in each of the solvents employed. The data from these reactions are summarized in Table I.

C. The Inverse Addition Acylation of Cyclopropane

In a 250-ml, one-necked flask equipped with a magnetic stirrer and pressure equalizing dropping funnel, a mixture of 6.66 g (0.050 mole) of aluminum chloride and 50 ml of

methylene chloride was stirred. Acetyl chloride (3.96 g, 0.050 mole) was slowly added to the reaction vessel and the mixture was stirred for 20 min. The pale green solution was filtered through scintered glass and kept dry in a one-necked flask fitted with a drying tube. Into a 300-ml, three-necked flask equipped with a stirrer, gas-inlet tube, pressure equalizing dropping funnel, and dry-ice condenser and cooled by means of a salt-ice bath was placed 50 ml of methylene chloride. Cyclopropane (29 ml, 21 g, 0.50 mole) was condensed in a trap cooled to -79^0 in a dry-ice/acetone mixture and slowly bubbled over a one-hour period into the three-necked flask. Finally the solution of acetylating reagent was dropped into the flask over a one-hour period at a rate that maintained the reaction temperature below 10^0, and the reaction mixture was stirred for an additional hour at $4-7^0$. During the time of addition and stirring the solution took on a very deep cherry-red color. The reaction mixture was slowly poured onto a mixture of 40 ml of concentrated hydrochloric acid and 100 g of crushed ice, and the organic layer was washed successively with 50-ml portions of water, 10% sodium bicarbonate solution, and water, and dried over anhydrous sodium sulfate. Product composition was determined by vpc analysis on a silicone column at 120^0 with the Helium pressure at 40 ml/min. It was found that the yield of 1,2-addition products was increased at the expense of the 1,1- and the "normal" 1,3-addition products. The results from

inverse addition in two solvents, methylene chloride and carbon tetrachloride, are summarized in Table III.

D. The Acylation of Cyclopropane with Added 5-Chloro-2-pentanone, 4-Chloro-3-methyl-2-butanone or 3-Chloro-2-pentanone

These reactions were carried out using normal acylating conditions except that known quantities of 5-chloro-2-pentanone, 4-chloro-3-methyl-2-butanone or 3-chloro-2-pentanone were added to the solvent prior to the addition of the acylating reagent. The results of these experiments are summarized in Table II.

E. The Acylation of Cyclopropane with Added Relatively Non-nucleophilic Bases

1. The Acylation of Cyclopropane with Added Tetrahydrofuran

Cyclopropane (2.1 g, 0.050 mole) was acetylated as previously described except that an equimolar amount of tetrahydrofuran was added to the methylene chloride solvent prior to the addition of acylating agent. After work-up, only the products formed in the normal acylation of cyclopropane (5-chloro-2-pentanone (17%), 4-chloro-3-methyl-2-butanone (47%), 3-methyl-3-butene-2-one (34%) and 3-chloro-2-pentanone (2%)) were detected by vpc analysis. There was no sign of acetylcyclopropane as checked by a comparison of the vpc retention time of an authentic sample of acetylcyclopropane.

2. The Acylation of Cyclopropane with Added 2,6-Lutidine

The acetylation of cyclopropane (0.4 g, 0.01 mole) with an equimolar amount of 2,6-lutidine added to the methylene chloride solvent prior to addition of the acetylating agent produced, along with the usual acylation products, no acetylcyclopropane as indicated by vpc analysis. 5-Chloro-2-pentanone was formed in 24%, 4-chloro-3-methyl-2-butanone was formed in 52%, 3-chloro-2-pentanone in 4%, and 3-methyl-3-butene-2-one in 20% yield.

3. The Acylation of Cyclopropane with Added N,N-Diisopropylethylamine

This experiment was identical to the inverse addition acylation of cyclopropane in methylene chloride except that an equimolar amount of N,N-diisopropylethylamine was added to a methylene chloride solution of cyclopropane (2.1 g, 0.050 mole) prior to the addition of the acylating solution. After work-up vpc analysis indicated that only the usual acylation products and no acetylcyclopropane had been produced. The yields as indicated by vpc were: 5-chloro-2-pentanone (8%), 4-chloro-3-methyl-2-butanone (42%), 3-chloro-2-pentanone (3%) and 3-methyl-3-butene-2-one (47%).

F. The Reaction of Cyclopropane with Acetyl Perchlorate

Into a 250-ml, one-necked flask equipped with a magnetic stirrer and drying tube was introduced anhydrous silver perchlorate (29 g, 0.14 mole) and acetyl chloride (11 g,

0.14 mole) in 200 ml of methylene chloride (50). The mixture was stirred for 20 min, the silver chloride filtered off, and the filtrate was placed in a 300-ml three-necked flask equipped with a magnetic stirrer, gas inlet tube, thermometer, and dry-ice condenser and externally cooled by means of an ice bath. Cyclopropane (7.2 ml, 5.0 g, 0.12 mole) was condensed in a trap cooled in a dry ice-acetone bath and was bubbled slowly (one hour) into the acetylating agent, and the resultant mixture was stirred for 1.5 hours at 3-7°. The clear, colorless solution was poured onto a mixture of 100 ml of concentrated hydrochloric acid and 250 g of crushed ice, and the organic layer was washed successively with water, 10% sodium carbonate solution three times (until neutral to pH paper) and water and dried over anhydrous sodium sulfate. The methylene chloride was stripped off via distillation and when the organic residue was transferred to a clean dry flask a violent explosion occurred (51).

G. Nmr Study of a Homogeneous Solution of Acetyl Chloride-Aluminum Chloride Complex and Cyclopropane in Carbon Tetrachloride

The procedure used was identical to that employed for the normal acylation of cyclopropane in carbon tetrachloride. A sample of the reaction mixture was placed in an nmr tube immediately after all of the cyclopropane was added to the acetylating reagent. The methyl doublet (J = 7.0 cps) of

$CH_3COCH(\underline{CH_3})CH_2Cl$ appeared at τ 8.62 before work-up and at τ 8.80 after hydrolysis. The methylene α- to the chlorine in $CH_3COCH_2CH_2\underline{CH_2}Cl$ appeared as a triplet (J = 6.0 cps) at τ 6.30 in the complex and at τ 6.42 in the isolated compound. Integration of the doublet of 4-chloro-3-methyl-2-butanone and the triplet of 5-chloro-2-pentanone gave (after statistical correction) a ratio of β/γ-chloroketone of 1.20:1; the vpc ratio after work-up was 1.17:1 (see Table I).

Separate experiments showed that 4-chloro-3-methyl-2-butanone is stable under the vpc conditions employed in this study. When a sample of 4-chloro-3-methyl-2-butanone was injected onto a column at the conditions normally used (130^0 at a Helium flow rate of 40 ml/min) there was no sign of 3-methyl-3-butene-2-one. Thus the β-chloroketone does not thermally dehydrohalogenate on the gas chromatograph.

III. Experiments with Acetylcyclopropane

A. The Reaction of Acetylcyclopropane with Hydrogen Chloride and Aluminum Chloride

In a 300-ml, three-necked flask equipped with a gas-inlet tube, mechanical stirrer, pressure equalizing dropping funnel, and dry ice condenser filled with liquid nitrogen, 6.66 g (0.050 mole) of anhydrous aluminum chloride and 38 ml of methylene chloride were stirred. Hydrogen chloride (1.5 ml, 1.8 g, 0.050 mole) was condensed in a trap cooled

with liquid nitrogen and was bubbled slowly into the reaction flask. Finally acetylcyclopropane (4.2 g, 0.050 mole) was slowly added to the solution which was cooled by means of an external ice bath. After the clear pale brown solution was stirred for 45 min, it was slowly poured onto a mixture of 40 ml of concentrated hydrochloric acid and 100 g of crushed ice. The organic layer was successively washed with 50-ml portions of water, 10% sodium bicarbonate solution, and water and dried over anhydrous sodium sulfate. Vpc analysis of the clear, pale yellow solution on a 5-foot SE-30 column at 120^0 with a Helium flow rate of 25 ml/min showed the presence of a single peak (ret. time = 3.2 min) which was shown to be identical (ret. time, ir and nmr spectra) with authentic acetylcyclopropane. There were no other peaks.

B. The Acylation of Cyclopropane with added Acetylcyclopropane

The procedure used was identical to that employed for the normal acylation of cyclopropane. An equimolar amount (compared to the acylating reagent and cyclopropane) of acetylcyclopropane was added to the acetyl chloride-aluminum chloride complex prior to the addition of the cyclopropane. After work-up, vpc analysis on a 5-foot FFAP column at 125^0 with a Helium flow rate of 45 ml/min indicated that all of the added acetylcyclopropane remained unchanged throughout the course of the reaction (see Table II).

C. The Acylation of Acetylcyclopropane

1. The Acylation of Acetylcyclopropane under Normal Conditions

The usual acylation procedure was used, except that the substrate, acetylcyclopropane, was added by means of a pressure equilibrating dropping funnel rather than via the gas-inlet tube used in the acylation of cyclopropane. After the addition of the acetylcyclopropane the reaction mixture was stirred for an additional hour at 3-6^0 before work-up. The gas chromatogram showed two peaks; one which proved to be unreacted starting material (92%) and the other (8%) represented some acylation product(s).

2. The Acylation of Acetylcyclopropane under Forcing Conditions

In a 250-ml, one-necked flask fitted with a magnetic stirrer and drying tube 13.33 g (0.100 mole) of anhydrous aluminum chloride was stirred in 20 ml of methylene chloride. A solution of acetyl chloride in 20 ml of methylene chloride was slowly dropped into the reaction flask, and the solution was stirred for 25 min. After stirring the acetylating reagent was filtered through scintered glass and was added as a clear, pale yellow solution into a 250-ml, three-necked flask equipped with a magnetic stirrer, thermometer, condenser, and pressure equalizing dropping funnel. A solution of acetylcyclopropane (8.4 g, 0.10 mole) in 40 ml of methylene chloride was added to the flask over a 25 min period while

the reaction temperature was maintained below 40^0, and the reaction mixture was stirred for an additional 48 hours at room temperature. During the addition of acetylcyclopropane and subsequent stirring the solution slowly acquired a fairly intense cherry-red color. The reaction mixture was poured onto a mixture of 55 ml of concentrated hydrochloric acid and 100 g of crushed ice, and the organic layer was washed with water, twice with saturated sodium bicarbonate solution, and water and the resultant clear, pale yellow solution was dried over anhydrous sodium sulfate. After removal of the solvent in vacuo vpc analysis indicated that about 40% of the acetylcyclopropane remained unreacted. Of the reacted material more than 95% proved to be a mixture of three chloroketones. These compounds were collected by preparative scale vpc and submitted to mass spectrometric analysis. Each of the compounds showed parent peaks at m/e = 162 and 164, corresponding to $C_7H_{11}O_2Cl$.

The first compound had a retention time of 1.2 min on a five foot Lexan (polycarbonate resin) column at 130^0 with a Helium flow rate of 80 ml/min and was formed in 30% yield. This compound had a complex group of bands in the ir spectrum (liquid film) centered at 1715 cm^{-1}. The compound was not further characterized.

The second chloroketone, formed in 33% yield, had a retention time of 2.9 min and had a sharp carbonyl stretch at 1715 cm^{-1}. The nmr spectrum (CCl_4 soln) consisted of a one proton triplet (J = 6.1 cps) at τ 6.40, a two proton

quartet (J = 6.1 cps) at τ 7.48, a six proton singlet at τ 7.88 and a complex two proton multiplet at τ 7.95. On the basis of these data 3-chloroheptane-2,6-dione is tentatively assigned as the structure.

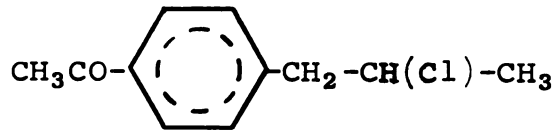
The third chloroketone had a retention time of 3.8 min and was formed in 32% yield. The ir spectrum (CCl_4 soln) showed the carbonyl band at 1710 cm^{-1}. The nmr spectrum (CCl_4 soln) had a multiplet accounting for two protons centered at τ6.42, a six proton singlet at τ 7.83, and a two proton multiplet at τ 7.80. A tentative structure of 3-chloromethylhexane-2,5-dione is assigned. The 12 line spectrum expected for the C-3 proton at about τ 7.2 does not appear in the nmr spectrum.

IV. The Acylation of Phenylcyclopropanes

A. The Normal Acylation of Phenylcyclopropane

The procedure employed was identical to that used for the normal acylation of cyclopropane, except that the phenylcyclopropane was added by means of a pressure equalizing dropping funnel rather than via the gas-inlet tube used in the acylation of cyclopropane. Vpc analysis indicated that two major products accounted for 95% of the completely reacted phenylcyclopropane. The major product (78% yield) had a retention time, ultraviolet and infrared spectra identical with those of authentic p-cyclopropylacetophenone, (31). The nmr spectrum (CCl_4 soln) of 31 consisted of an

aromatic A_2B_2 system centered at τ 2.10 (two lines) and at τ 2.73 (two lines , J = 8.5 cps) accounting for four protons, a three proton singlet at τ 7.42 for the methyl ketone, and a pair of multiplets at τ 8.07 and τ 8.93 for the cyclopropyl hydrogens. The other major product (17% yield) was determined to be 1-(4-acetylphenyl)-2-chloropropane, (32), on the basis of its spectral properties. Its ir spectrum



32

(liquid film) showed principal bands at 1685 ($\nu_{C=O}$), 1607 ($\nu_{C=C}$) and 752 cm^{-1} (ν_{C-Cl}). The nmr spectrum (CCl_4 soln) consisted of an aromatic A_2B_2 system (J = 8.5 cps) at τ 2.25 (two lines) and at τ 2.87 (two lines) for four protons, a sharp three proton resonance at τ 7.51 for the methyl ketone group, a complex multiplet centered at τ 6.98 for the methylene protons, and a methyl doublet (J = 7.2 cps) at τ 8.52. The ultraviolet spectrum (95% EtOH) showed λ_{max} 250 mμ (log ε 4.11); literature value for p-methylacetophenone (52) λ_{max} 252 mμ (log ε 4.18).

B. The Acylation of p-Cyclopropylacetophenone

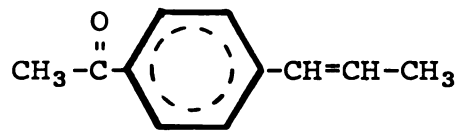
Normal acylation of p-cyclopropylacetophenone (3.20 g, 0.0200 mole) at a reaction temperature of 30° led to 85% recovered starting material and 15% of a product identical

(ret. time and ir spectrum) with 1-(4-acetylphenyl)-2-chloropropane (32) after one hour. After 24 hours there was about 50% conversion of the starting material, as monitored by vpc, and continued reaction led to the formation of polymeric material.

C. The Reaction of p-Cyclopropylacetophenone with Sulfuric Acid

In a 100-ml, one-necked flask equipped with a dropping funnel and a magnetic stirrer, 1.0 g (0.0063 mole) of p-cyclopropylacetophenone and 10 ml of methylene chloride were stirred. Sulfuric acid (80%, 15 ml) was added over a 15 min period, and the ensuing dark brown solution was stirred for an additional 15 min and then slowly poured onto 100 g of crushed ice. The organic layer was extracted with 50 ml of methylene chloride and dried over anhydrous sodium sulfate. After removal of the solvent in vacuo, 0.93 g (93% yield) of a pale yellow oil was obtained. This oil was pure according to vpc analysis and was identified as 1-(4-acetylphenyl)-1-propene (33) on the basis of its spectral properties. The principal ir bands (liquid film) appeared at 1680 ($\nu_{C=O}$), 1650 ($\nu_{C=C}$), and 1603 cm^{-1} ($\nu_{C=C}$). The nmr spectrum (CCl_4 soln) showed the presence of an aromatic A_2B_2 system centered at τ 2.23 (two lines) and at τ 2.77 (two lines) (J = 8.5 cps) for four protons, a multiplet for the allylic methyl centered at τ 8.18, a sharp singlet at τ 7.57 for the methyl ketone protons, a

one proton multiplet centered at τ 3.75 assigned to the α-styryl proton resonance, and a complex multiplet centered at τ 4.82 for the β-styryl proton. The ultraviolet spectrum (95% EtOH) showed λ_{max} 286 mμ; literature value (53), λ_{max} 280 mμ for p-acetylstyrene.



33

V. The Acylation of 1,1-Dimethylcyclopropane

The usual procedure for acylating a liquid substrate was followed. The reaction was carried out on a 0.10 molar scale (7.0 g of 1,1-dimethylcyclopropane) in methylene chloride for 45 min at 5°. After work-up, vpc analysis indicated the presence of two products; 4-chloro-3,4-dimethyl-2-pentanone (78% yield) and 3,4-dimethyl-3-pentene-2-one (22% yield).

The structure of 4-chloro-3,4-dimethyl-2-pentanone was clear from its spectral properties. Its infrared spectrum (liquid film) showed principal bands at 1710 ($\nu_{C=O}$), 1370 and 1390 ($\nu_{(CH_3)_2C}$), and 760 cm^{-1} (ν_{C-Cl}). The nmr spectrum (CCl_4 soln) consisted of a quartet (J= 7.0 cps) at τ 7.01 for the methine proton adjacent to the carbonyl function, a three proton resonance at τ 7.79 for the methyl ketone

protons, a sharp six proton singlet at τ 8.34 for the gem-dimethyl group, and a methyl doublet (J = 7.0 cps) at τ 8.79.

The identity of the α,β-unsaturated ketone was determined from its ir and nmr spectra. The infrared spectrum (CCl_4 soln) showed absorbances indicative of an α,β-unsaturated ketone at 1680 ($\nu_{C=O}$) and 1625 cm^{-1} ($\nu_{C=C}$). The nmr spectrum (CCl_4 soln) showed three singlets at τ 7.95, 8.17, and 8.27 in the area ratio 1:2:1. The two high field resonances were slightly broadened due to long range coupling.

A separate experiment showed that treatment of 1.0 g (0.0066 mole) of 4-chloro-3,4-dimethyl-2-pentanone with a 20% solution of sodium carbonate (20 ml, 4 g, 0.04 mole) for 15 min at reflux in 15 ml of carbon tetrachloride led to a clean conversion to 0.67 g (0.0060, 91%) of 3,4-dimethyl-3-pentene-2-one.

VI. The Acylation of 1,1,2-Trimethylcyclopropane

The procedure employed was identical to that used in the preceding experiment. After work-up, only one major product (80% yield) was observed upon vpc analysis. The structure of the product, 4-chloro-3,3,4-trimethyl-2-pentanone was confirmed by ir and nmr spectroscopy. The infrared spectrum (CCl_4 soln) showed a sharp carbonyl band at 1700 cm^{-1}. The nmr spectrum (CCl_4 soln) consisted of three sharp singlets at τ 7.82, 8.42 and 8.75 in the

area ratio 1:2:2, assigned to the methyl ketone protons, the α-chloro dimethyl protons, and the 3,3-dimethyl protons respectively.

A separate experiment showed that treatment of 10 ml of a carbon tetrachloride solution of 60 mg (3.7×10^{-3} mole) of 4-chloro-3,3,4-trimethyl-2-pentanone with 10 ml of a 20% solution of sodium carbonate (2 g, 0.02 mole) for 15 min at reflux led only to the recovery of unchanged starting material.

VII. The 2-Ethyl-1,1-dimethylcyclopropane System

A. The Preparation of 2-Ethyl-1,1-dimethylcyclopropane

The carbene used to prepare this compound was generated according to the method of LeGoff (54). To a hot (nearly refluxing) solution of 0.25 g of cupric acetate monohydrate in 25 ml of glacial acetic acid in a 250-ml, one-necked flask, 18 g (0.28 mole) of 30-mesh granular zinc was added. The mixture was shaken for two min, keeping it hot during this period to prevent precipitation of zinc acetate. The acetic acid was decanted and the couple was washed with a 25-ml portion of glacial acetic acid. After decanting the acid and cooling the flask, the reagent was washed with two 50-ml portions of anhydrous ether. The flask containing the couple was then fitted with a reflux condenser, magnetic stirrer and dropping funnel, and 50 ml of anhydrous ether was added. Next a few drops of methylene iodide

were added, and after brief warming a reaction began (bubbles rose from the couple). While the mixture was kept at gentle reflux a solution of 16.8 g (0.20 mole) of 2-methyl-2-pentene and the remainder of the methylene iodide (total of 75.2 g, 0.22 mole) was added dropwise over a period of 50 min. The reaction mixture was stirred at reflux for 36 hours. The dark, milky purple solution was slowly decanted from the unchanged Zn-Cu couple into a one-liter separatory funnel containing 40 ml of 1N hydrochloric acid and 50 g of crushed ice. A slight evolution of gas accompanied this step. The ethereal solution was separated, filtered and washed with two 75-ml portions of 1N hydrochloric acid and crushed ice and with three 75-ml portions of water and the clear, colorless solution was dried over anhydrous potassium carbonate.

Distillation on a stainless steel spinning band column afforded 6.0 g (0.061 mole) of a clear, colorless compound boiling at 76-78^0/740 mm. This compound proved to be (ir and nmr spectra) 2-ethyl-1,1-dimethylcyclopropane. The ir spectrum (CCl_4 soln) had bands indicative of the cyclopropyl ring at 3080 and 980 cm^{-1}. The nmr spectrum (neat) consisted of a 6 proton singlet at τ 8.73 for the gem-dimethyl group and the rest of the protons appeared in a complex spectrum from τ 7.90 to τ 9.90.

B. The Acylation of 2-Ethyl-1,1-dimethylcyclopropane

The usual procedure for acylating a liquid substrate was employed. The reaction was carried out on a 0.0050 molar scale (0.49 g of 2-ethyl-1,1-dimethylcyclopropane) in 10 ml of methylene chloride for 45 min at 5^0. Stannic chloride was used as the Lewis acid. The reaction was monitored by vpc and the reaction mixture was found to consist of at least seven products, a mixture that proved intractable to clean separation.

C. The Acylation of 2,3-Dimethyl-2-pentene

The procedure used was identical to that employed in the preceding experiment. The reaction was monitored by vpc and a mixture of at least seven products was observed. A comparison of the vpc traces (10 foot SE-30 column at 155^0 with a Helium flow rate of 35 ml/min) from the acylations of 2-ethyl-1,1-dimethylcyclopropane and 2,3-dimethyl-2-pentene indicated that the reaction mixtures were virtually identical.

VIII. The Acylation of Methylcyclopropane

Since methylcyclopropane is a gas (bp 4^0) this acylation was run using the procedure outlined for the normal acylation of cyclopropane. Methylcyclopropane (Chemical Procurement Laboratories) was purified by slowly passing it through a trap containing saturated, neutral potassium

permanganate solution, then through a trap containing anhydrous calcium sulfate (Drierite) and collecting the gas in a vessel cooled in a dry-ice/acetone bath. The resultant material was tested by vpc and found to be pure. A 0.10 molar scale reaction (5.5 g of methylcyclopropane) in 50 ml of methylene chloride was carried out at 0^0 for one hour. The reaction was monitored by vpc using a 5 foot QF-1 column at 130^0 with a Helium flow rate of 70 ml/min. Three major components with retention times of 0.70, 3.0, and 4.0 min were observed.

The compound with the retention time of 0.70 min was formed in 12% yield and was found to be a clear, colorless liquid. It was shown to be identical with the unsaturated ketone formed in the acylation of 2-butene; i.e., 3-methyl-3-pentene-2-one. The ir spectrum (CCl_4 soln) had principal bands at 1670 ($\nu_{C=O}$) and 1640 cm^{-1} ($\nu_{C=C}$). The nmr spectrum (C_6D_6 soln) showed a quartet of quartets (J_{gem} = 7.0 cps, J_{vic} = 1.4 cps) at τ 3.68 for the vinyl proton, a singlet at τ 8.00 for the methyl ketone protons, a three proton multiplet centered at τ 8.25 (C-3 methyl group), and an eight line resonance at τ 8.58 for the remaining methyl group.

The second product had a retention time of 3.0 min and was formed in 18% yield. The structure was shown to be 4-chloro-3-methyl-2-pentanone on the basis of its ir and nmr spectra. The carbonyl band in the ir spectrum (CCl_4 soln) appeared at 1710 cm^{-1}. The nmr spectrum (CCl_4 soln)

consisted of a one proton multiplet centered at τ 5.80 (C-4 proton), a one proton multiplet at τ 7.32 (C-3 proton), a singlet for the methyl ketone protons at τ 7.82, a doublet (J = 6.5 cps) at τ 8.50 (C-4 methyl) and a doublet (J = 7.0 cps) at τ 8.87 (C-3 methyl).

The major product was formed in 65% yield, had a retention time of 4.0 min, and was shown to be 5-chloro-2-hexanone by its ir and nmr spectra. The ir spectrum (CCl_4 soln) had the carbonyl stretch at 1710 cm^{-1}. The nmr spectrum (CCl_4 soln) showed a one proton multiplet centered at τ 6.02 (methine proton), a triplet (J = 7.0 cps) at τ 7.38 for the two protons adjacent to the carbonyl function, a singlet at τ 7.92 for the methyl ketone protons, a complex multiplet centered at τ 8.08 for the C-4 methylene protons, and a doublet (J = 6.5 cps) at τ 8.48 for the C-6 methyl protons.

RESULTS AND DISCUSSION

Cyclopropane

Addition of cyclopropane at 0^0 to a homogeneous 1:1 acetyl chloride-aluminum chloride complex in chloroform resulted in the formation, after work-up, of four products (Eq. 9). These products were carefully separated and

(9) $CH_3COCl + H_2C\overset{CH_2}{\diagdown\diagup}CH_2 \xrightarrow[CHCl_3]{AlCl_3}$ $CH_3COCH_2CH_2CH_2Cl$ (23±2%) **34**

+

$CH_3COCH(CH_3)CH_2Cl$ (42±3%) **35** + $CH_3COC(CH_3)=CH_2$ (31±3%) **36**

+

$CH_3COCH(Cl)CH_2CH_3$ (4±1%) **37**

purified by preparative scale vapor phase chromatography. In the previous work (34), the reaction mixture decomposed upon distillation and consequently was dehydrohalogenated with a 20% solution of sodium carbonate at reflux prior to product isolation. Previously (34), 3-methyl-3-butene-2-one, (**36**), was identified and characterized as its 2,4-DNP derivative, and the prior formation of 4-chloro-3-methyl-2-butanone, (**35**), was inferred. Authentic 5-chloro-2-pentanone and the acylation product **34** gave identical derivatives (34). The minor product, 3-chloro-2-pentanone, (**37**), was not observed. In the present work, structure proof for all four products was based on their ir, nmr and mass spectra. In

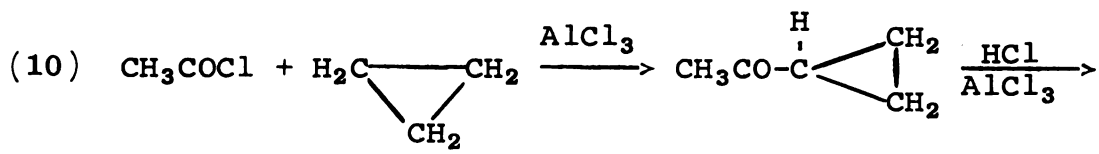
addition, an unambiguous synthesis of 37 was carried out (see Experimental).

The acylation of cyclopropane was shown to proceed readily in other Friedel-Crafts acylation solvents (carbon tetrachloride, methylene chloride, carbon disulfide, and nitrobenzene) and in all cases afforded the three rearrangement products, 35, 36, and 37 along with the expected 5-chloro-2-pentanone.

Subjection of the homogeneous acylation reaction mixture in carbon tetrachloride solvent to direct nmr examination at room temperature led to the discovery that all four reaction products were present prior to work-up. The ratio of 4-chloro-3-methyl-2-butanone, (35), to 5-chloro-2-pentanone, (34), found by nmr was 1.20:1; the vpc ratio after work-up was 1.17:1. This not only verified the reliability of the vpc method, but also established that 3-methyl-3-butene-2-one, (36), is formed directly during the course of the acylation and not by dehydrohalogenation of the β-chloroketone during the work-up procedure. Separate experiments affirmed that indeed 35 was not dehydrohalogenated under the employed vpc conditions.

Several experiments were performed to determine whether 4-chloro-3-methyl-2-butanone, (35), and/or 3-chloro-2-pentanone, (37), are formed directly in the acylation of cyclopropane, or whether they arise *via* some indirect pathway. It is conceivable, for example, that formation of acetylcyclopropane followed by reaction with hydrogen chloride

(in the presence of the Lewis acid, aluminum chloride) might lead to the observed mixture of chloroketones. Although ring opening to the β- and/or γ-chloroketone does not seem likely (Eq. 10), acetylcyclopropane was treated with aluminum chloride and hydrogen chloride in methylene chloride

(10) 

$CH_3COCH_2CH_2CH_2Cl$ + $CH_3COCH(CH_3)CH_2Cl$ + $CH_3COCH(Cl)CH_2CH_3$

34 35 36

at 5^0 for one hour. Vpc analysis showed a single peak which proved to be identical (ret. time, ir and nmr spectra) with the starting material. Acetylcyclopropane was also found not to suffer ring opening in the acylating medium at 0^0 either in the presence or absence of cyclopropane. Indeed, the reaction of acetylcyclopropane with acetyl chloride and aluminum chloride at room temperature for 48 hours (approximately 60% reaction) led to three chloroketones whose parent peaks in the mass spectrometer each appeared at m/e = 162 and 164 ($C_7H_{11}O_2Cl$). Thus it is established that acetylcyclopropane cannot be a reaction intermediate in the acylation of cyclopropane.

Another possibility is that the α- and β-chloroketones are formed by some rearrangement of the normal γ-chloroketone, 5-chloro-2-pentanone, during the course of the acylation of cyclopropane (Eq. 11). Experimental results

(11) $CH_3COCH_2CH_2CH_2Cl \xrightleftharpoons{AlCl_3} CH_3COCH(CH_3)CH_2Cl$

$AlCl_3$ ↘ ↗ $AlCl_3$

$CH_3COCH(Cl)CH_2CH_3$

indicate that this postulate for the mode of formation of the abnormal products is also incorrect. Levitt (35) stirred 5-chloro-2-pentanone in chloroform at 0-10° for one hour with a four-fold excess of a 1:1 acetyl chloride-aluminum chloride complex (thus reproducing all of the conditions of acylation except for the cyclopropane). The γ-chloroketone was recovered unchanged in 80% yield and no evidence for the formation of any of the other acylation products was found.

The acylation of cyclopropane was carried out in the presence of known quantities of initially added 3-chloro-2-pentanone, 4-chloro-3-methyl-2-butanone, or 5-chloro-2-pentanone. The data in Table II show that the chloroketones are recovered unchanged in each case and hence are not interconverted during the reaction.

Any mechanism which begins with the formation of a classical carbonium ion (e.g., (38), with or without stabili-

$$CH_3-\overset{\overset{O}{\|}}{C}-CH_2-CH_2-CH_2^+$$

38

zation by the carbonyl oxygen seems doomed to a series of irrational subsequent steps to account for the formation of

Table I. The acylation of cyclopropane in various solvents

Solvent	Yield (%)			
	5-Chloro-2-pentanone	4-Chloro-3-methyl-2-butanone	3-Methyl-3-butene-2-one	3-Chloro-2-pentanone
CCl_4	35 ± 1[a]	40 ± 1	21 ± 1	4 ± 1
CS_2	38 ± 5	28 ± 4	25 ± 4	9 ± 1
$CHCl_3$	23 ± 2	42 ± 3	31 ± 3	4 ± 1
CH_2Cl_2	25 ± 1	53 ± 2	17 ± 3	5 ± 1
$C_6H_5NO_2$	18 ± 2	48 ± 3	30 ± 3	5 ± 1

[a]Yields are the average of at least two runs. Relative areas were obtained by multiplying the peak width at half height by the height and also by cutting out the peak traces and weighing them on a Mettler balance.

the abnormal products. The formation of a protonated cyclopropane in a scheme similar to that proposed by Baird and Aboderin (28) leads to the ready formation of both the anticipated 5-chloro-2-pentanone, and of the otherwise unexpected products, 4-chloro-3-methyl-2-butanone, 3-methyl-3-butene-2-one, and 3-chloro-2-pentanone (Scheme VII).

SCHEME VII

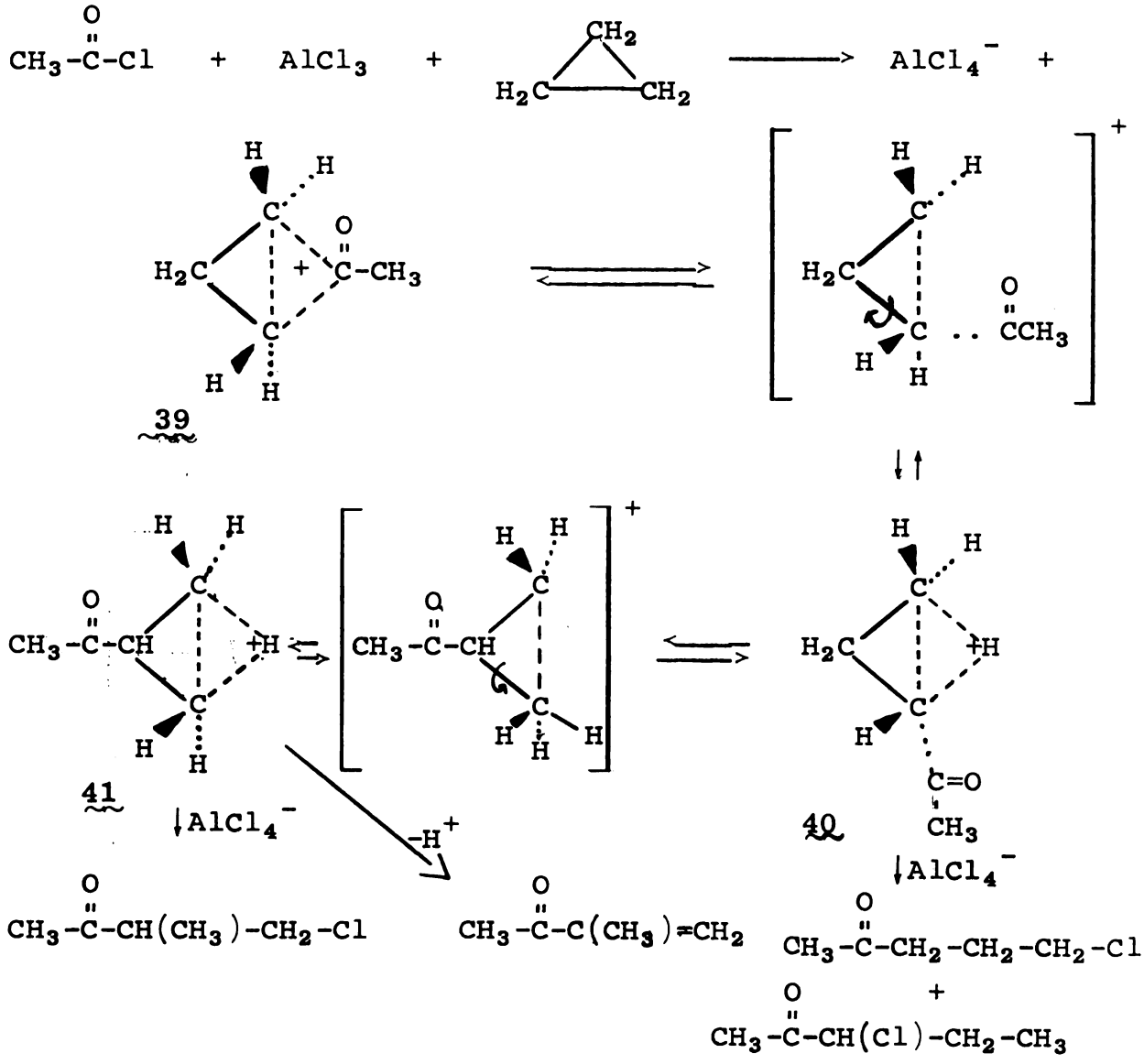
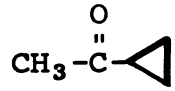
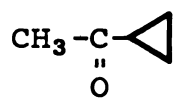


Table II. Cyclopropane acylation with added chloroketones or acetylcyclopropane

 (Mol)	Solvent	Added Reactant (Mol)	Products	Normal	Expected	Observed (Vpc)
0.010	CCl_4	34,	34	35	55	57
		0.0044	35	40	28	24
			36	21	14	16
			37	4	3	3
0.005	CCl_4	35,	34	35	36	38
		0.0017	35	40	55	48
			36	21	16	20
			37	4	3	4
0.010	CH_2Cl_2	37,	34	25	15	16
		0.0077	35	53	31	28
			36	17	10	11
			37	5	44	45
0.050	CH_2Cl_2		34	25	12	11
		0.050	35	53	28	32
			36	17	8	7
			37	5	2	2
				-	50	48

With the positive charge away from the carbonyl group, 41 should be a more stable species than 40. Consequently most of the reaction product should be derived from 41. The data in Table I support this hypothesis in all cases; i.e., the ratio of 4-chloro-3-methyl-2-butanone + 3-methyl-3-butene-2-one to 5-chloro-2-pentanone + 3-chloro-2-pentanone is, in every solvent, greater than one. Furthermore, even a larger proportion of product would be derived from 41 if the concentration of nucleophile were kept small to allow time for the conversion of the first formed ion 40 to the more stable 41. Slow addition of the acetyl chloride-aluminum chloride complex to a solution of cyclopropane (inverse addition) increased the yields of 4-chloro-3-methyl-2-butanone and 3-methyl-3-butene-2-one at the expense of the α- and γ-chloroketones. Table III compares the results of normal vs. inverse addition in the acylation of cyclopropane in methylene chloride and carbon tetrachloride.

The electrophilic nature of the acylation reaction is demonstrated by the rate retardation effect on the reaction by the presence of electron-withdrawing substituents on the cyclopropyl moiety (Table IV). Because of this fact, it is reasonable to postulate that the formation of 40 or its probable immediate precursor 39 is the rate-determining step in this reaction.

It should be noted that aside from Lee's work on the formolysis of 1-propyl tosylate-1-^{14}C (41), the data from the acylation of cyclopropane are the best evidence for a

Table III. Comparison of the normal and inverse addition acylations of cyclopropane

Solvent	Yield (Vpc)	
	Normal	
	4-Chloro-3-methyl-2-butanone + 3-Methyl-3-butene-2-one	5-Chloro-2-pentanone + 3-Chloro-2-pentanone
CCl_4	61 ± 1[a]	39 ± 1
CH_2Cl_2	70 ± 1	30 ± 1
	Inverse	
CCl_4	77 ± 2	23 ± 2
CH_2Cl_2	94 ± 1	6 ± 1

[a]See footnote, Table I.

Table IV. The retarding effect of electron-withdrawing substituents on the rate of cyclopropane acylation

Substituent	Solvent	Temp.	Reaction Time Hr.	Extent of Reaction %
None	$CHCl_3$	0^0	1	100
Cl- (35)	$CHCl_3$	25^0	18	100
1,1-di-Cl-(35)	$CHCl_3$	61^0	1	33
$CH_3-\overset{O}{\overset{\|}{C}}-$	$CHCl_3$	0^0	1	8
$CH_3-\overset{O}{\overset{\|}{C}}-$	CH_2Cl_2	25^0	48	60

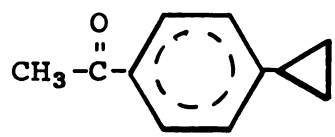
sequence of protonated cyclopropanes in a reaction path. Moreover, whereas only 1-2% of the formolysis reaction proceeds via protonated cyclopropanes (41), bridged ions apparently are formed from each cyclopropane molecule acylated.

While the present work was in progress, it was learned that the Lewis acid-catalyzed bromination of cyclopropane (55) afforded products which were unexpected on the basis of classical cyclopropane chemistry. Along with the expected product 1,3-dibromopropane, and 1,2-dibromopropane (which might arise from the possibly first formed ion, $BrCH_2CH_2CH_2^+$, via a 1,2-hydride shift mechanism), 1,1-dibromopropane was also found to be a minor reaction product. The formation of the 1,1-addition product cannot be easily rationalized by any mechanism involving classical carbonium ions, but can be readily derived along with the other products if a protonated cyclopropane intermediate is invoked.

The standard textbook mechanism for electrophilic attack on cyclopropane (56) thus is seen to be incomplete. Sulfation (28) and bromination (55) of cyclopropane along with the data presented here on the acylation of cyclopropane (57) provide powerful evidence which rules out simple Markownikov addition in this system. Postulation of protonated cyclopropanes affords a mechanistic rationalization which readily accounts for the formation of the observed 1,1- and 1,2-addition products, along with the "textbook" 1,3-addition product.

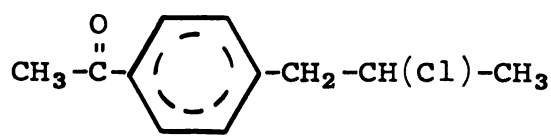
Phenylcyclopropane

In order to determine the scope of the applicability of the postulated bridged ion mechanism, the acylation of several substituted cyclopropanes was investigated. To establish the effect of an aromatic substituent on the cyclopropyl moiety, the acylation of phenylcyclopropane was examined. The Friedel-Crafts acetylation of phenylcyclopropane first resulted (35) in a 48% yield of p-cyclopropylacetophenone, (31). The structure of 31 had been deduced from the facts that chromic acid oxidation followed by esterification with methanol gave dimethyl terephthalate, establishing the para orientation, and hypobromite oxidation gave p-cyclopropylbenzoic acid in 88% yield. Ten percent



31

of a product, (32), whose structure was not elucidated was also formed. When the reaction was run at -75° Russian workers (58) reported that 31 was obtained in over 90% yield. When phenylcyclopropane (2.66 g, 0.020 mole) was acetylated in methylene chloride at 0° for one hour, a 75% yield of 31 and a 15% yield of 32 were obtained. Study



32

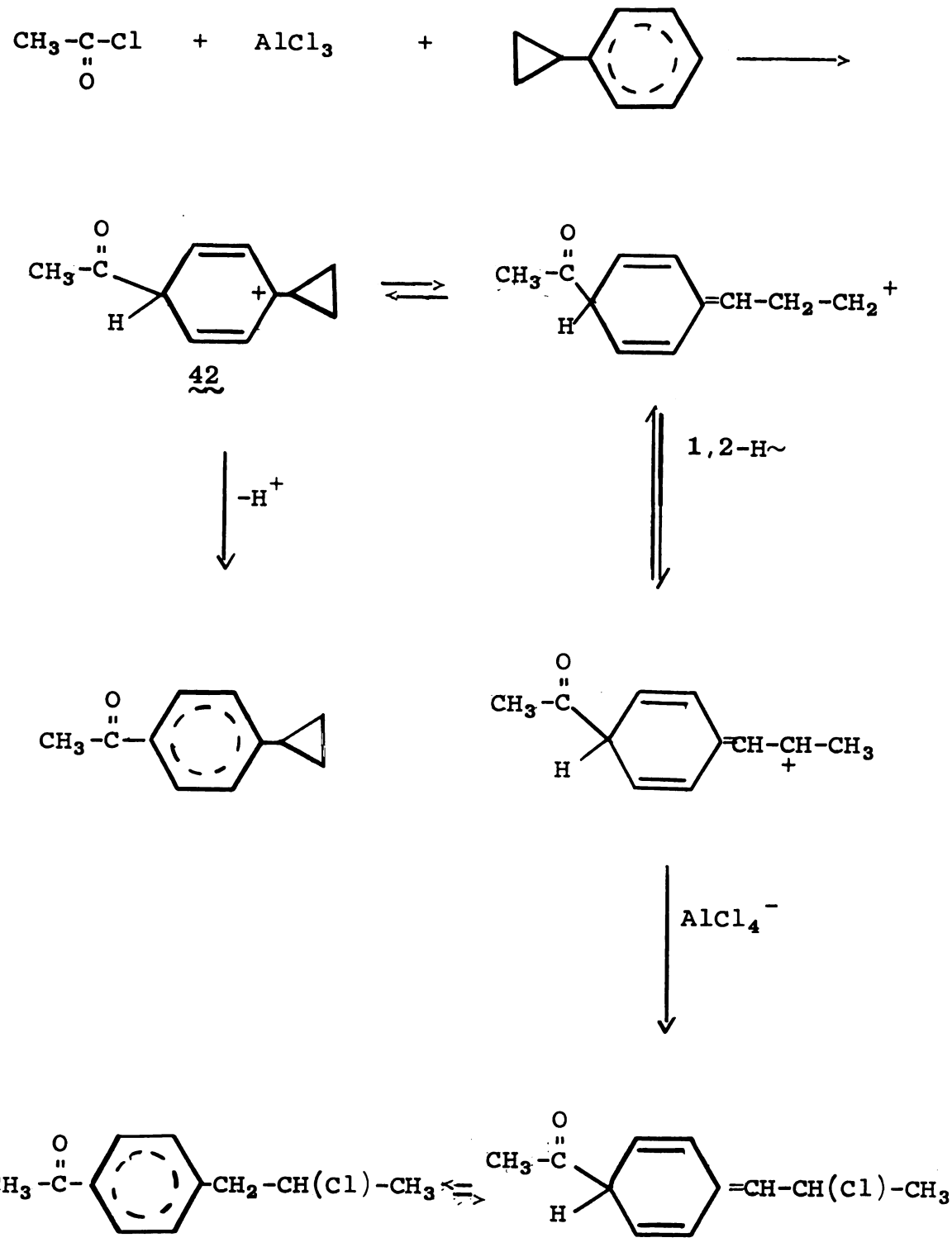
of the minor component by ir, nmr and uv techniques showed that the structure of 32 was 1-(4-acetylphenyl)-2-chloropropane. In the nmr spectrum the four aromatic protons appeared as an A_2B_2 system (J = 8.5 cps) at τ 2.25 and 2.87, the methyl ketone protons at τ 7.51, the methine proton at τ 8.07 (multiplet), the methylene protons at τ 6.98 (doublet, J = 7.2 cps) and the C-3 methyl at τ 8.52 (doublet, J = 7.2 cps).

Thus it is demonstrated that the aromatic ring is preferentially acylated. Attack of an acyl cationic species at the para position generates an electron deficient species, (42), which can collapse to give both 31 and 32 (Scheme VIII). Separate experiments showed that acylation of p-cyclopropylacetophenone also leads to the formation of 32. Hence it can not yet be determined whether 32 is a primary acylation product of phenylcyclopropane or whether it is an acylation product of p-cyclopropylacetophenone.

1,1-Dimethylcyclopropane

When 1,1-dimethylcyclopropane was acetylated by Levitt (35) a 59% yield of a single product, 4-chloro-3,4-dimethyl-2-pentanone, (43), was obtained. This reaction was re-examined with the aid of vpc. The β-chloroketone (43) was formed in 80% yield and the dehydrohalogenation product, 3,4-dimethyl-3-pentene-2-one, (44), was formed in 15% yield.

SCHEME VIII



$CH_3-\overset{O}{\overset{\|}{C}}-CH(CH_3)-C(CH_3)_2-Cl$ **43**

$CH_3-\overset{O}{\overset{\|}{C}}-C(CH_3)=C(CH_3)_2$ **44**

The ir spectrum of **44** had bands at 1680 and 1625 cm^{-1} for the α, β-unsaturated ketone group. Its nmr spectrum consisted of three singlets at, τ 7.95, 8.17 and 8.27 in the area ratio 1:2:1. Separate experiments showed that refluxing **43** with 20% sodium carbonate solution for 15 min led to a facile dehydrohalogenation to **44**. No sign of the expected 1,3-addition product, 5-chloro-5-methyl-2-hexanone, (**45**), was observed, nor was the 1,1-addition product, 3-chloro-4,4-dimethyl-2-pentanone, (**46**), found. The reaction of

$CH_3-\overset{O}{\overset{\|}{C}}-CH_2-CH_2-C(CH_3)_2-Cl$ **45**

$CH_3-\overset{O}{\overset{\|}{C}}-CH(Cl)-C(CH_3)_3$ **46**

2-methyl-2-butene with acetyl chloride-aluminum chloride complex was reported to yield the same β-chloroketone, (**43**), obtained in this study.

It is known that cyclopropane does not isomerize to propylene prior to acylation; propylene when acylated yielded 4-chloro-2-pentanone, (**47**), and 3-pentene-2-one, (**48**), (59), products not observed in the acylation of

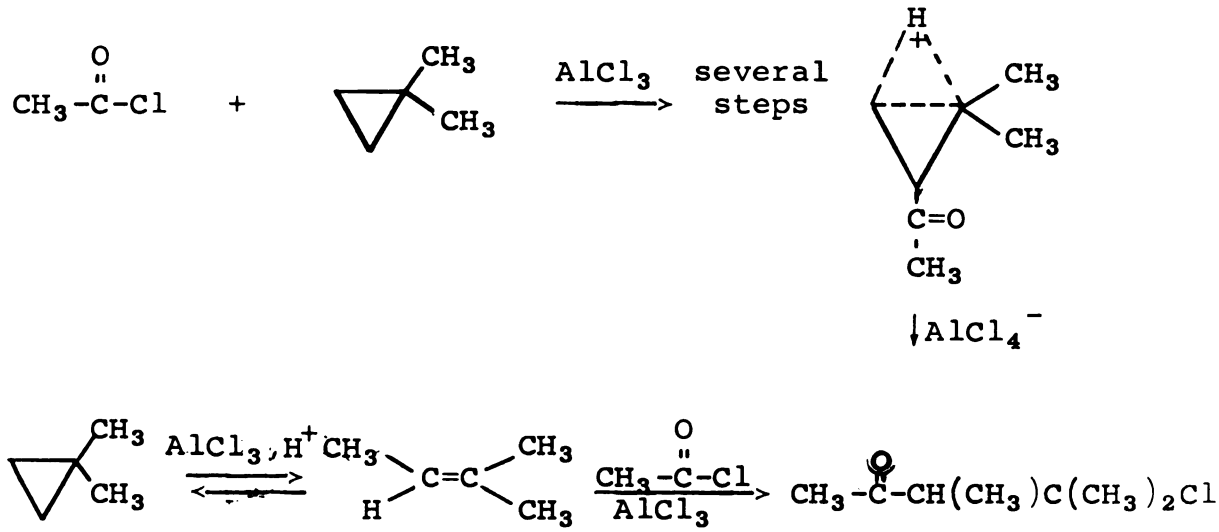
$CH_3COCH_2CH(Cl)CH_3$ **47**

$CH_3COCH=CHCH_3$ **48**

cyclopropane. However, the results with 1,1-dimethylcyclopropane and 2-methyl-2-butene suggest an alternative method

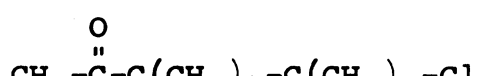
by which 43 and 44 might be formed; that is, the 1,1-dimethylcyclopropane might isomerize to 2-methyl-2-butene prior to acylation (Scheme IX).

SCHEME IX



1,1,2-Trimethylcyclopropane

A similar argument can be brought to bear upon the cases of 1,1,2-trimethylcyclopropane and of 2,3-dimethyl-2-butene. Acylation of either compound furnished the same chloroketone, (49), in over 80% yield. This product did not dehydrohalogenate when refluxed in 20% sodium carbonate solution and was identified as 4-chloro-3,3,4-trimethyl-2-pentanone by ir and nmr analysis. The nmr spectrum of 49



49

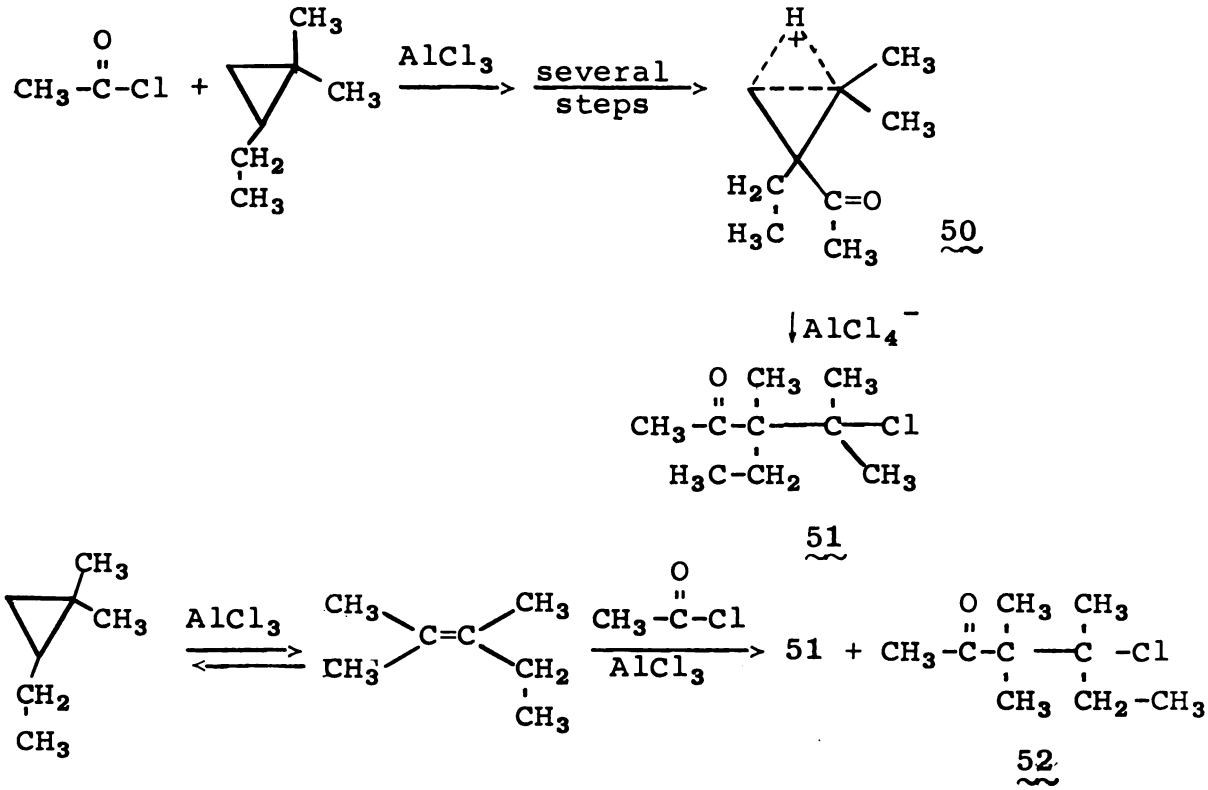
consisted of three sharp singlets at τ 7.82, 8.42 and 8.75 in the area ratio 1:2:2. These were assigned to the methyl

ketone protons, the α,chloro dimethyl protons, and the 3,3-dimethyl protons respectively. An increase in the refractive index of 1,1,2-trimethylcyclopropane over aluminum chloride has been attributed to both isomerization and polymerization (60). Other workers (61) report the very rapid and complete polymerization of 1,1-dimethylcyclopropane in the presence of aluminim bromide even at -50°, the reaction being complete within a few minutes.

2-Ethyl-1,1-dimethylcyclopropane

In an attempt to determine which alternative mechanism is applicable in the acylation of polyalkyl-substituted cyclopropanes, 2-ethyl-1,1-dimethylcyclopropane was investigated. Scheme X indicates that if 2-ethyl-1,1-dimethylcyclopropane is acetylated via a bridged ionic intermediate (50), only 4-chloro-3-ethyl-3,3,4-trimethyl-2-pentanone, (51), would be expected as a major product. If, however, the cyclopropane isomerized to 2,3-dimethyl-2-pentene prior to the acylation reaction, both 51 and 4-chloro-3,3,4-trimethyl-2-hexanone, (52), would be expected to be furnished in approximately equal amounts. Acylation of 2-ethyl-1,1-dimethylcyclopropane or 2,3-dimethyl-2-pentene using either aluminum chloride or stannic chloride as the Lewis acid led to a very complicated reaction mixture, with the formation of a large number of products. No single product was formed in over 20% yield according to vpc analysis, and the entire reaction mixture from either substrate quickly polymerized and decomposed upon standing. Identical acylations

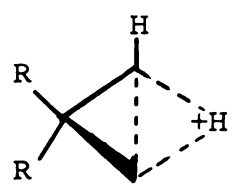
SCHEME X



of 2-ethyl-1,1-dimethylcyclopropane and 2,3-dimethyl-2-pentene in methylene chloride using stannic chloride as the Lewis acid (thereby obtaining the cleanest reaction mixture after work-up) led to the formation of seven products. The reactions were monitored by vpc and the gas chromatograms from the two reaction mixtures (i.e., the cyclopropane and the olefin) were virtually identical. From these data it can be concluded that polyalkyl-substituted cyclopropanes appear to isomerize to the corresponding stablest olefins prior to acylation.

In systems where the classical carbonium ion structure would be primary (n-propyl or cyclopropane precursor) or would be otherwise destabilized, Baird (28) suggested that

hydrogen-bridged intermediates (edge-protonated cyclopropanes) would be most important. On the other hand, in substituted systems, Wagner-Meerwein rearrangment, classical carbonium ions, or carbon-bridged structures should be favored over hydrogen-bridged species. Karabatsos (22) averred that protonated cyclopropanes are involved to approximately 5% in the nitrous acid deamination of 1-propylamine, to less than 1% in the deaminations of 1-butylamine and isobutylamine, and were not observed in the case of neopentylamine. He suggested that these results were brought about because of the greater stability of the classical carbonium ions (relative to the bridged ionic intermediate) in the substituted systems, and steric repulsions which would arise upon formation of an intermediate such as 55.



55

A similar trend is seen in the acylation of cyclopropane. Cyclopropane acylates entirely via protonated cyclopropanes. In sharp contrast, 1,1-dimethylcyclopropane, 1,1,2-trimethylcyclopropane, and 2-ethyl-1,1-dimethylcyclopropane apparently isomerize to the corresponding olefins prior to acylation.

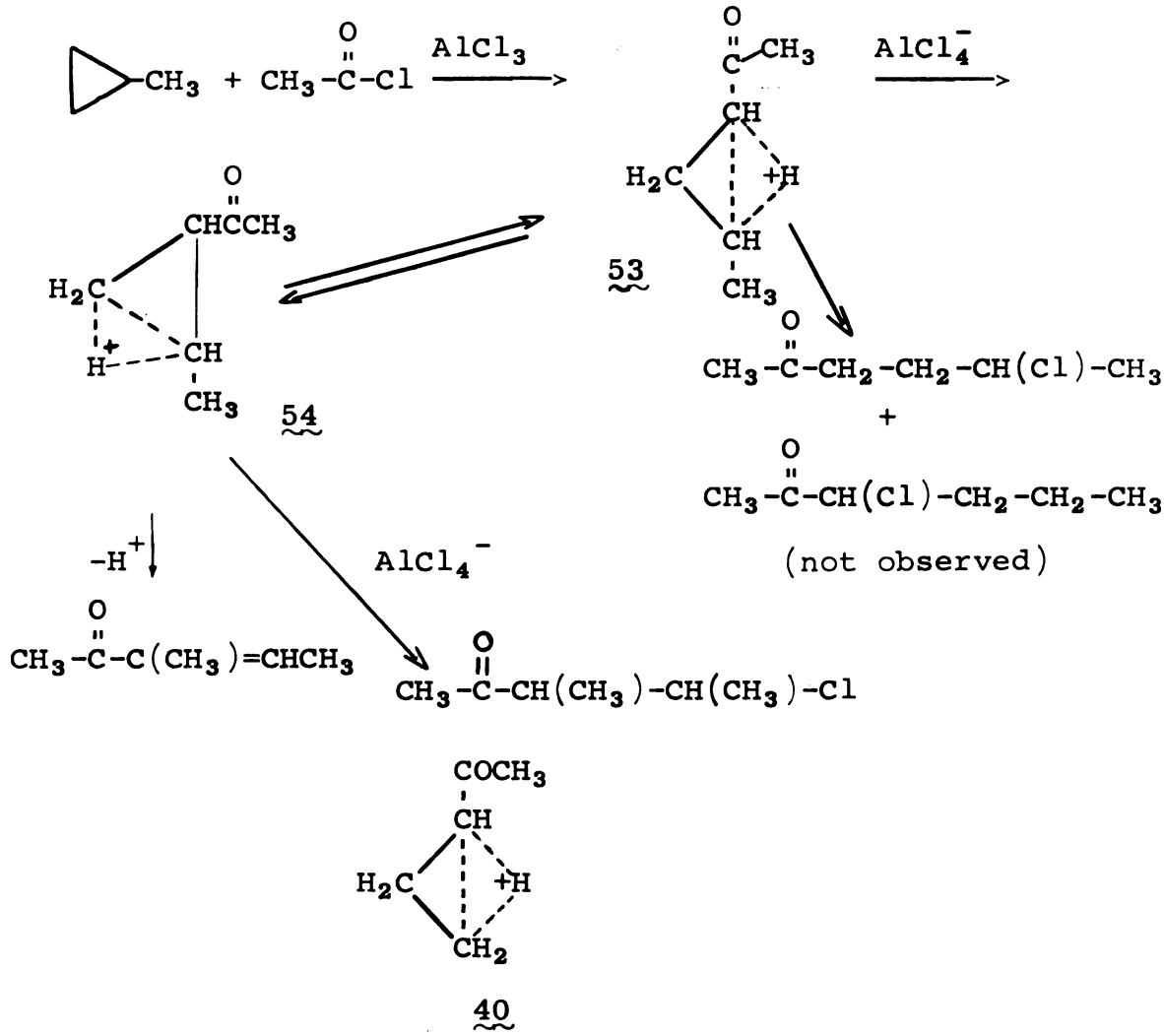
It seemed worthwhile to investigate a monoalkylcyclopropane, to determine which of the two possible reaction paths would be followed.

Methylcyclopropane

The acylation of methylcyclopropane led to the formation of 5-chloro-2-hexanone (65% yield), 4-chloro-3-methyl-2-pentanone (12% yield) and 3-methyl-3-pentene-2-one (14%). The nmr spectrum of the major product, 5-chloro-2-hexanone, consisted of a one proton multiplet at τ 6.02 (methine proton), a triplet (J = 7.0 cps) at τ 7.38 for the methylene protons α- to the carbonyl group, a singlet at τ 7.92 for the methyl ketone protons, a multiplet at τ 8.08 for the C-4 methylene protons and a doublet (J = 6.5 cps) at τ 8.48 for the C-6 methyl protons. The nmr spectrum of 4-chloro-3-methyl-2-pentanone had a multiplet at τ 5.80 (C-4 proton), a multiplet at τ 7.32 (C-3 proton), a singlet at τ 7.82 (methyl ketone protons), a doublet (J = 6.5 cps) at τ 8.50 (C-4 methyl) and a doublet for the C-3 methyl protons at τ 8.87 (J = 7.0 cps). The nmr spectrum of the α, β-unsaturated ketone showed a quartet of quartets (J_{gem} = 7.0 cps, J_{vic} = 1.4 cps) at τ 3.68 (vinyl proton), a singlet at τ 8.00 (methyl ketone protons), a multiplet for the C-3 methyl group at τ 8.25 and an eight line resonance for the remaining methyl group at τ 8.58.

Whereas the 1,2-addition products may arise either from a bridged intermediate or from prior isomerization of

the methylcyclopropane to 2-butene, the 1,3-addition product cannot reasonably arise from 2-butene. The formation of bridged intermediate 53 would lead to 5-chloro-2-hexanone and subsequent equilibration to ion 54 would lead to the formation of the other two products. Ion 53 is more stable than the corresponding ion from the acylation of cyclopropane, 40, and hence a greater percentage of the total product should be derived from 53 than from 40; this was in fact observed (~70% vs ~30-40%).



SUMMARY

1. The acylation products of cyclopropane with acetyl chloride-aluminum chloride complex in chloroform at 0^0 were 4-chloro-3-methyl-2-butanone (42%), 3-methyl-3-butene-2-one (31%), 5-chloro-2-pentanone (23%) and 3-chloro-2-pentanone (4%). The overall yield of acylated product was 96%.

2. 1,1-dimethylcyclopropane with acetyl chloride at 0^0 furnished 4-chloro-3,4-dimethyl-2-pentanone, identical with the product from 2-methyl-2-butene and acetyl chloride, in 78% yield and 3,4-dimethyl-3-pentene in 22% yield.

3. 1,1,2-Trimethylcyclopropane with acetyl chloride at 0^0 produced only 4-chloro-3,3,4-trimethyl-2-pentanone (80%), identical with the product from 2,3-dimethyl-2-butene.

4. The product mixtures from the reaction of acetyl chloride with 2-ethyl-1,1-dimethylcyclopropane and 2,3-dimethyl-2-pentene were virtually identical according to vpc analysis.

5. Treatment of methylcyclopropane in the acylating medium led to the formation of 5-chloro-2-hexanone (65%), 4-chloro-3-methyl-2-pentanone (18%), and 3-methyl-3-pentene-2-one (12%).

6. Phenylcyclopropane was smoothly acylated at 0^0 to p-cyclopropylacetophenone (72% yield) and 1-(4-acetylphenyl)-2-chloropropane (15%).

7. Acetylcyclopropane did not suffer ring opening under normal acylation conditions, nor did it react with hydrogen chloride and aluminum chloride in methylene chloride at 5^0.

8. The mechanism of the acylation of cyclopropane and substituted cyclopropanes has been discussed in the light of these results. Cyclopropane acylates entirely via protonated cyclopropanes, as apparently does methylcyclopropane. The most likely structure for these ions is the "edge-protonated" form (see Introduction, Part C). In sharp opposition to these results, 1,1-dimethylcyclopropane, 1,1,2-trimethylcyclopropane, and 2-ethyl-1,1-dimethylcyclopropane apparently isomerize to stable tri- or tetrasubstituted olefins prior to acylation.

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APPENDIX

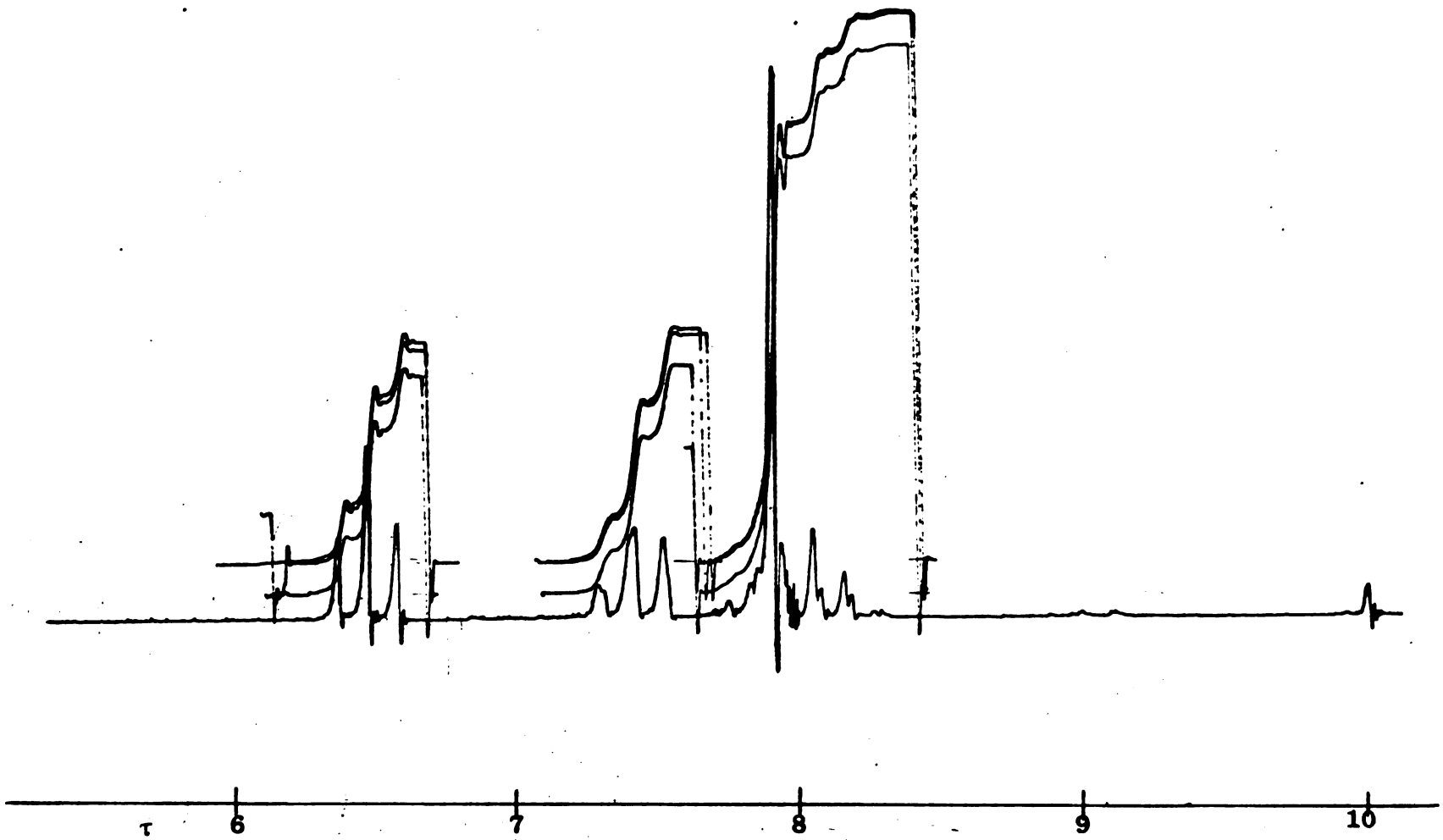


Figure 1. Proton magnetic resonance spectrum of 5-chloro-2-pentanone (CCl_4 soln).

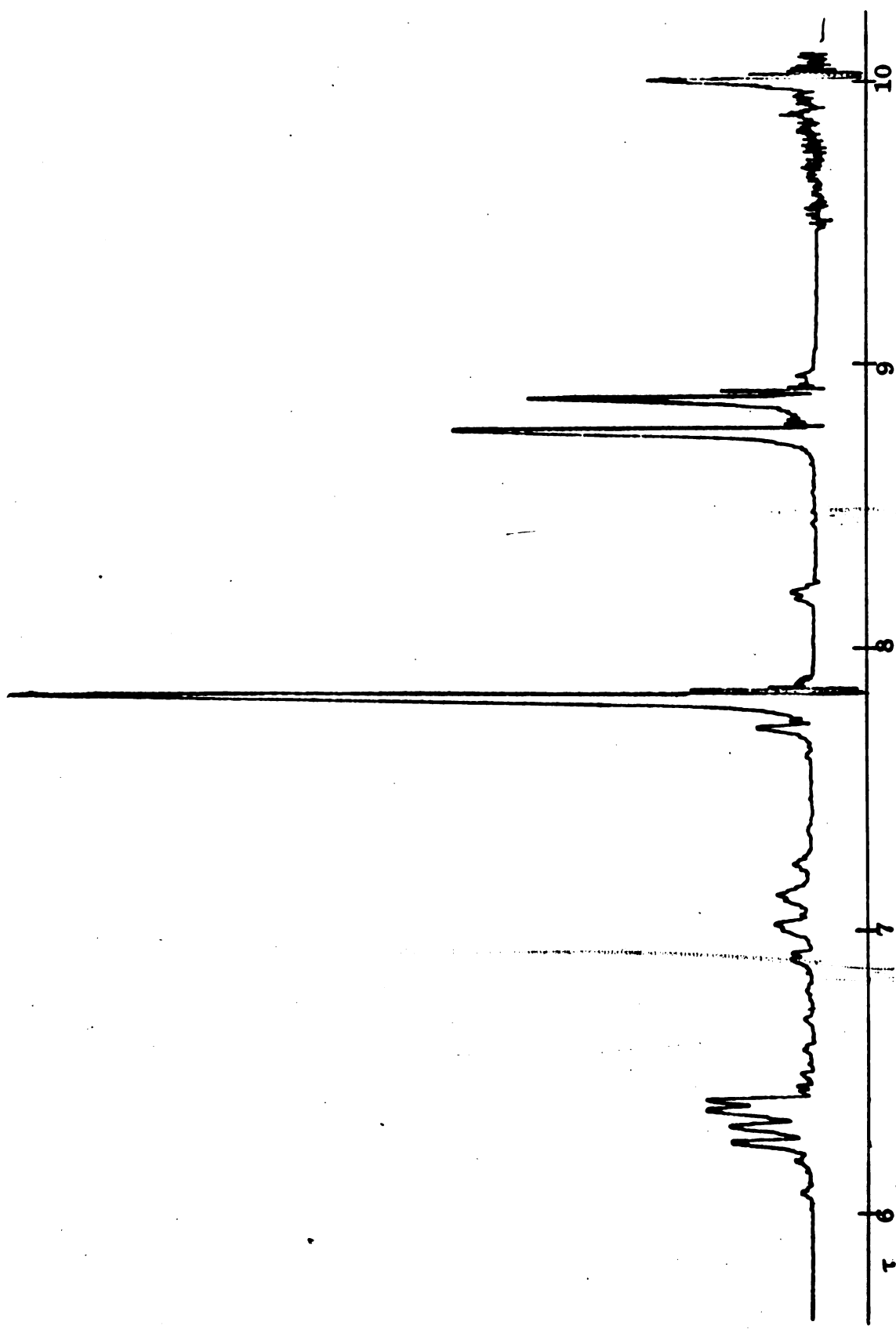


Figure 2. Proton magnetic resonance spectrum of 4-chloro-3-methyl-2-butanone (CCl_4 soln).

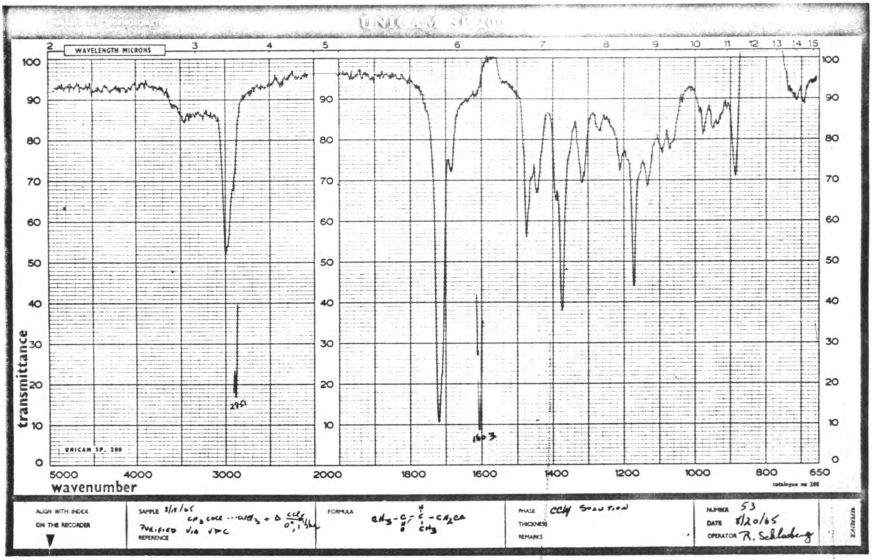
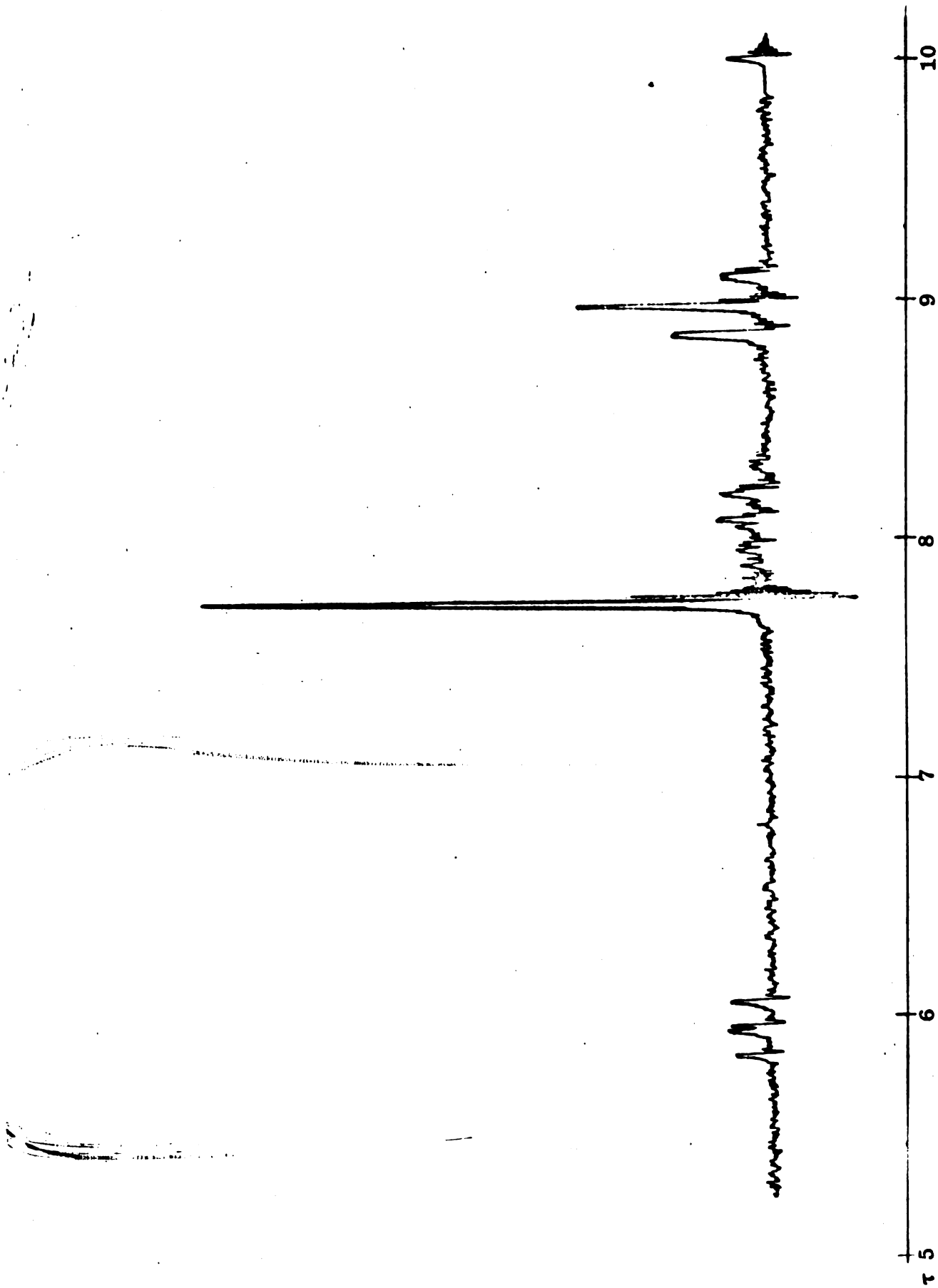


Figure 3. Infrared spectrum of 4-chloro-3-methyl-2-butanone.



re 4. Proton magnetic resonance spectrum of 3-chloro-2-pentanone (CCl_4 soln).

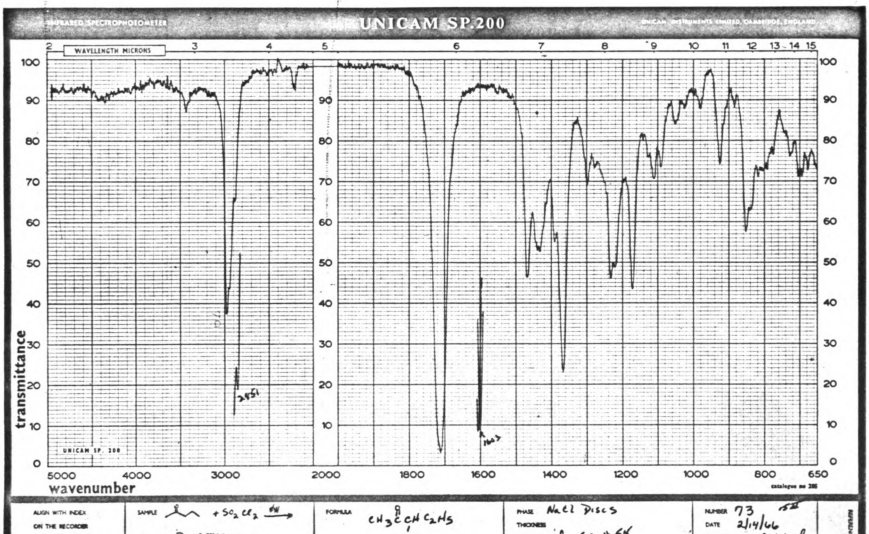


Figure 5. Infrared spectrum of 3-chloro-2-pentanone.

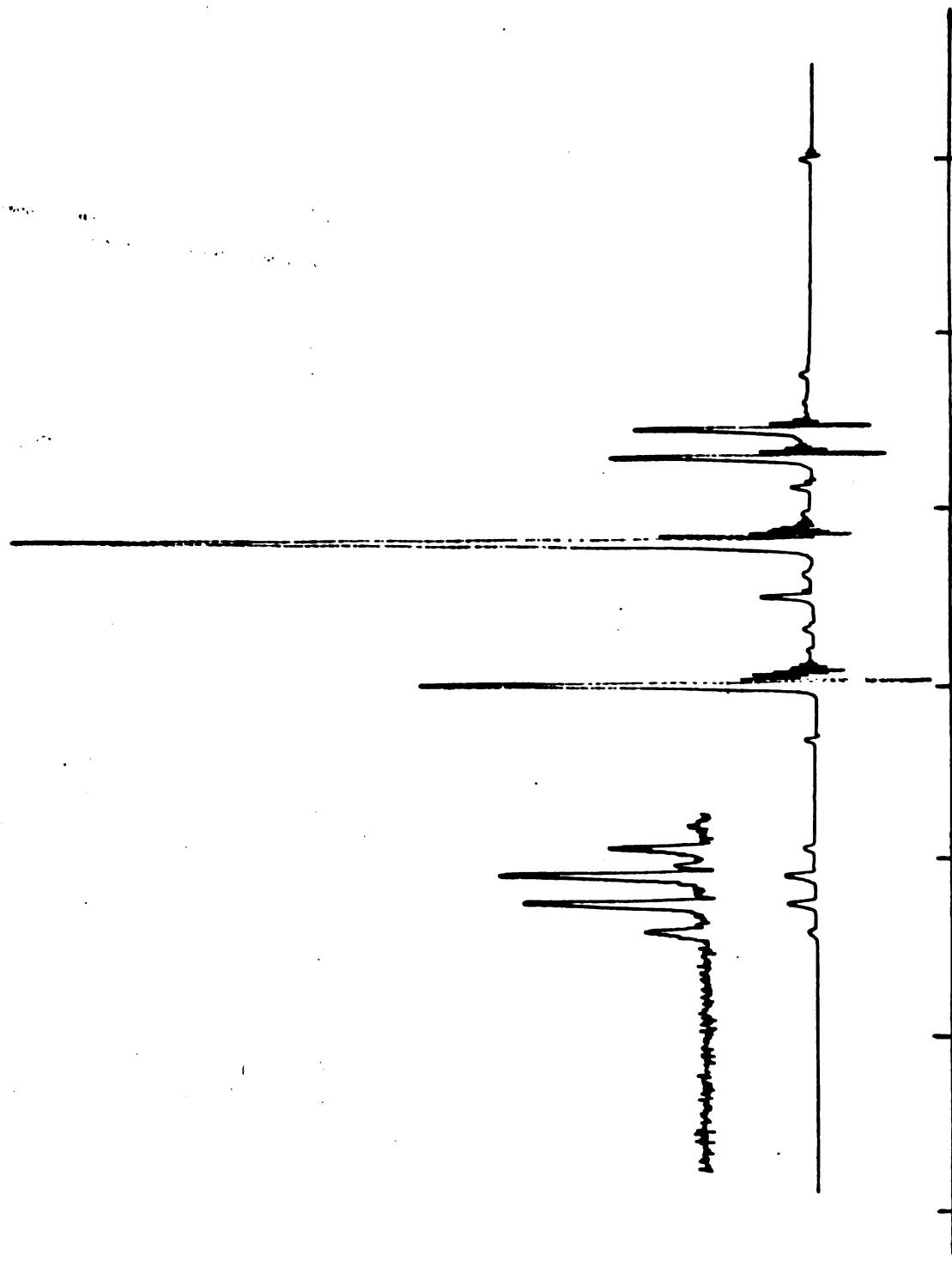


Figure 6. Proton magnetic resonance spectrum of 4-chloro-3,4-dimethyl-2-pentanone (CCl_4 soln).

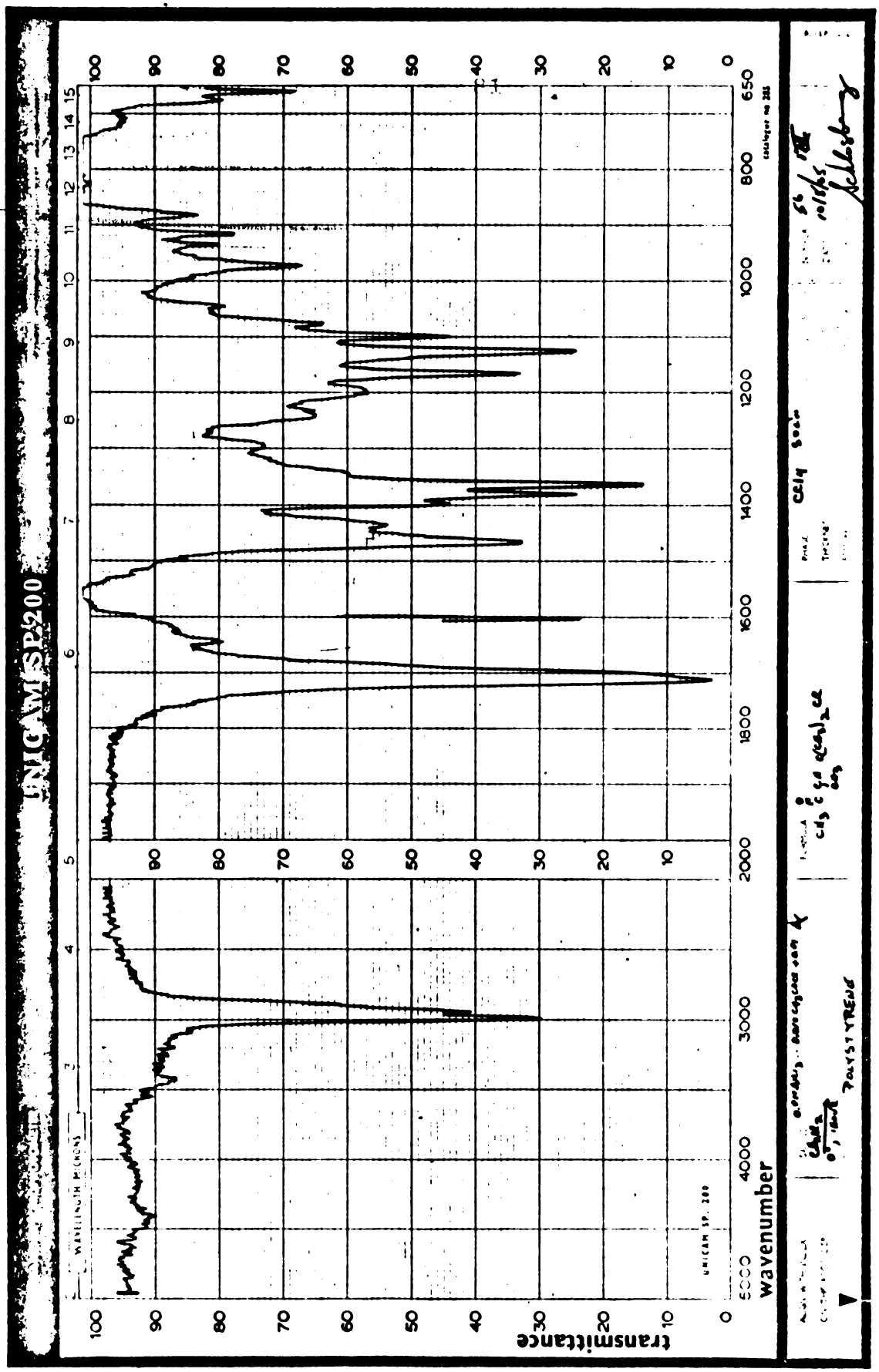


Figure 7. Infrared spectrum of 4-chloro-3,4-dimethyl-2-pentanone.

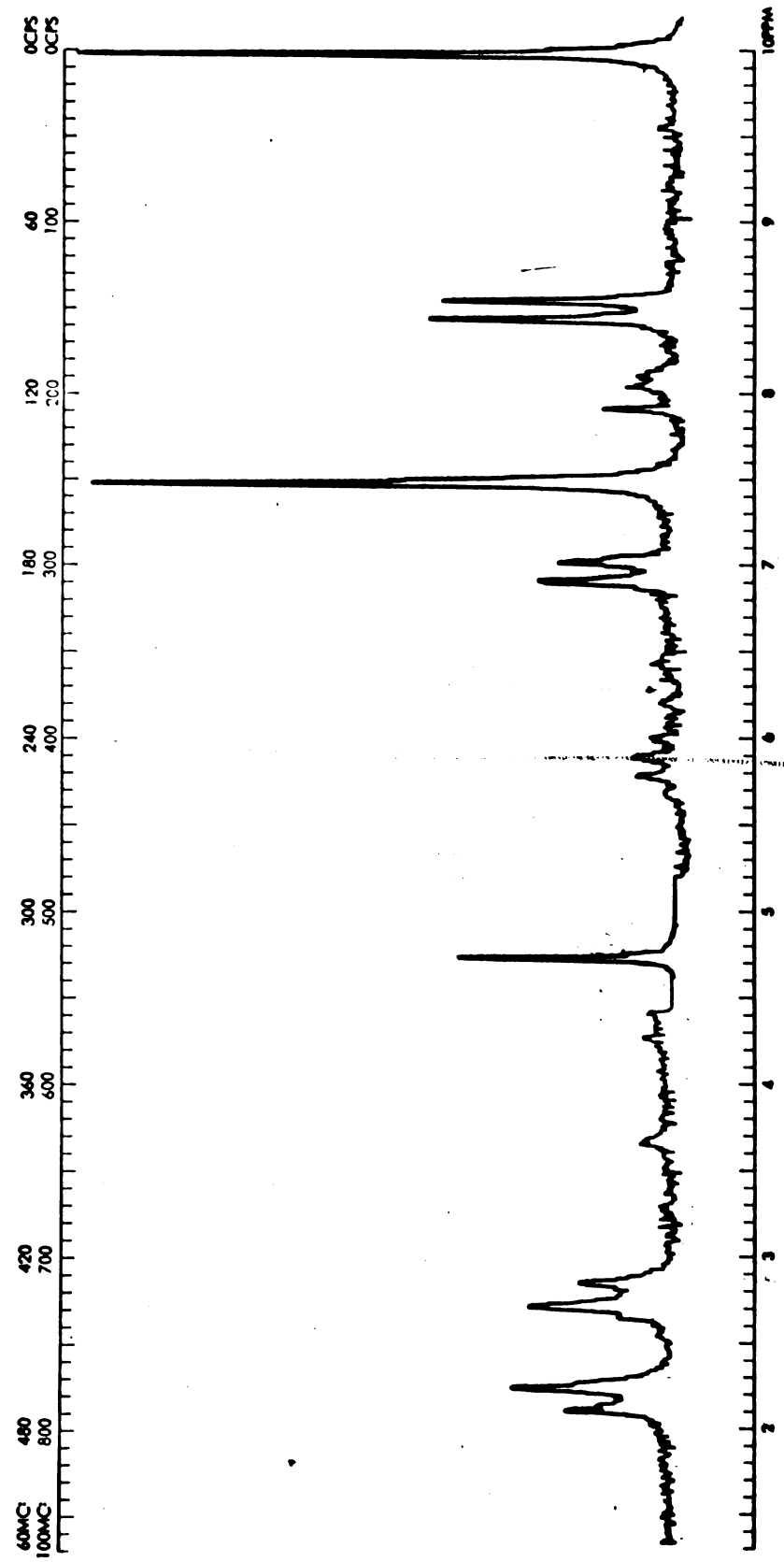


Figure 8. Proton magnetic resonance spectrum of 1-(4-acetylphenyl)-2-chloropropane (CCl_4 soln).

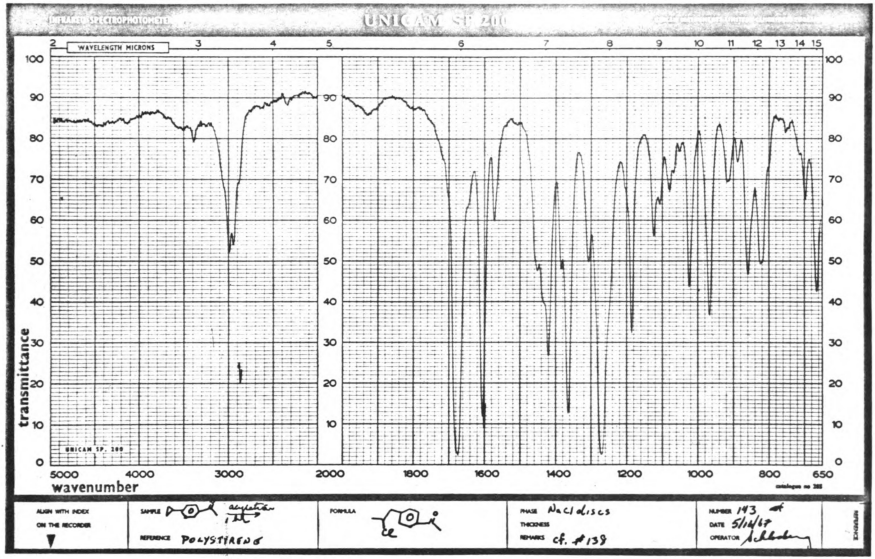


Figure 9. Infrared spectrum of 1-(4-acetylphenyl)-2-chloropropane.